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American Journal of Diseases of Children

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CUTANEOUS REACTIONS TO HEMOLYTIC STREPTOCOCCUS NUCLEOPROTEIN IN PERSONS WITH SCARLET FEVER

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AND

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NEW YORK

Hypersensitiveness of the skin to products of hemolytic streptococci has been studied by numerous investigators. In most instances the tests have been made with filtrates. With such complex antigens the difficulties in interpreting reactions are obvious. Derrick and Fulton [1] have reported on cutaneous reactivity to various bacterial nucleoproteins in patients with a variety of diseases. Ando and Ozaki [2] have reported the results of cutaneous tests with nucleoprotein from Streptococcus scarlatinae in a group of 860 patients. The tests to be reported here were performed with purified hemolytic streptococcus nucleoprotein and were carried out on patients with an infection known to be caused by the hemolytic streptococcus, which causes scarlet fever. For controls, 617 children in the wards of the Babies Hospital who did not have scarlet fever, rheumatic fever or nephritis were tested. While these studies were being carried out at the Willard Parker Hospital, Gibson and McGibbon [3] published their work on the same problem in England. Their results are discussed later.

From the Willard Parker Hospital, the Departments of Medicine and Pediatrics, College of Physicians and Surgeons, Columbia University, and the Babies Hospital.

1. Derrick, C., and Fulton, M.: Skin Reactions of Patients and Normal Individuals to Protein Extracts of Streptococci, J. Clin. Investigation **10**:121, 1931.

2. Ando, K., and Ozaki, K.: Studies on the Toxins of Hemolytic Streptococci: The Dick Test and Allergic Skin Reactions to Streptococcus Nucleoproteins, J. Immunol. **18**:267, 1930.

3. Gibson, J. J., and McGibbon, J. P.: An Allergic Skin Reaction After Scarlet Fever, Lancet **2**:729, 1932.

METHOD OF MAKING THE TEST AND INTERPRETING THE REACTION

The nucleoprotein was prepared by Heidelberger and Kendall from a scarlatinal strain of Streptococcus haemolyticus by a method described by them in 1931.[4] Fraction K was used in testing the patients with scarlet fever and the majority of patients in the control group. This fraction is the hemolytic streptococcus protein precipitable by acetic acid (after the removal of less alkaline extracts) between p_H 11 and 13.3. The nucleoprotein was made up in physiologic solution of sodium chloride so that 0.1 cc., the amount used for cutaneous tests, contained 0.001 mg. of nitrogen.

All tests were made intradermally in the skin of the forearm. Occasionally in infants the thigh was used. Exactly 0.1 cc. from a tuberculin syringe was injected. After twenty-four hours the areas of erythema and induration were measured, and the reaction was graded from zero to ++++. The positive reaction is similar to that of the Mantoux tuberculin test and not at all like the Dick reaction. There is a central, deeply red, indurated area surrounded by a zone of erythema of variable intensity and size. Ordinarily there is no constitutional reaction. In the subjects with the more severe progressive reactions the entire arm is warm, swollen and painful; occasionally the local reaction may exhibit formation of vesicles or even necrosis. The usual reaction begins to fade after from thirty-six to forty-eight hours and disappears in a few days. Severe reactions may persist from one to two weeks.

The following criteria were used in recording results: negative reaction, erythema of less than 10 mm. diameter and induration of less than 5 mm. diameter; positive reaction (+ to ++), erythema of from 10 to 30 mm. diameter with induration of from 5 to 15 mm. diameter, and strongly positive reaction (+++ to ++++), erythema of from 30 to 100 mm. diameter with induration in proportion.

In the appraisal of the degree of reaction induration was regarded as having greater significance than the area of erythema. The category ++++ was reserved for large progressive reactions with marked induration or for those in which there was formation of vesicles.

RESULTS

Thirty-two children were tested at weekly intervals after the onset of scarlet fever for a period of thirty days; 20 of these children were retested from two to nine months later. Thirty-one children were between the ages of 5 and 12 years and one child was 20 months old. The scarlet fever was mild or moderate in severity. Six patients were regarded as ill enough to warrant the administration of antitoxin, but no patient suffered from disease of the toxic or fulminant type. In 11 cases there were pyogenic complications, chiefly otitis media, cervical adenitis and mastoiditis. Nephritis developed in 1 patient, and 1 child who had a low grade fever from the twentieth to the thirtieth day of the disease was later discovered at another clinic to have rheumatic carditis. Slight transient fever with negative results of physical examination was not considered a complication.

4. Heidelberger, M., and Kendall, F. J.: Protein Fractions of a Scarlatinal Strain of Streptococcus Hemolyticus, J. Exper. Med. **54**:515, 1931.

The table has been constructed on the basis of the most strongly positive reaction exhibited by each patient during several periods after the onset of the disease. Of 26 patients tested in the first week of the disease 3 gave a positive reaction on the fifth, sixth and seventh day, respectively, and 23 gave a negative reaction. The entire group of 32 patients gave a positive reaction by the thirtieth day. Six gave a negative reaction after the first week, three on the eighth day and 1 each on the tenth, eleventh and fourteenth days. All subsequently gave a positive reaction. Each of the 20 patients who were tested from two to nine months after the onset of scarlet fever gave a positive reaction. The 6 children who were given scarlet fever antitoxin did not react differently from the others.

The effect of complications (otitis media, mastoiditis, cervical adenitis) on the reaction to nucleoprotein was interesting. In the period from eight to thirty days after the onset 18 children gave a

Cutaneous Reactions to Hemolytic Streptococcus Nucleoproteins in Patients with Scarlet Fever *

	Days After Onset		
	3 to 7	8 to 30	80 to 270
Strongly positive	0	18	8
Positive	3	14	12
Negative	23	0	0

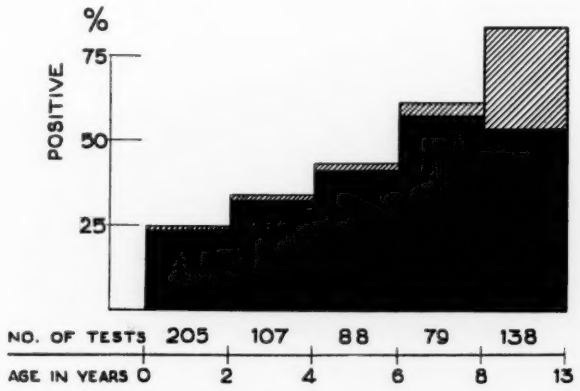
* Multiple tests were carried out on all the patients, but only the strongest reaction in the individual patient in each period after the onset of disease is given here.

strongly positive reaction; 9 of these children had complications. Among 14 moderately positive reactions, only 2 occurred in children who had complications. In the follow-up period, of 8 strongly positive reactions, 3 occurred in children with complications, and of 12 moderate reactions only 3 occurred in children with complications. There is, then, a tendency for the strongly positive reactions to occur in cases of scarlet fever with complications.

It would be interesting to know how long this sensitivity persists. In an attempt to get information on this point 28 children who gave a history of scarlet fever were tested. In 5 cases the date of the scarlet fever was not recorded; in the others the test was carried out from six weeks to ten years after the onset. In 19, or 67.8 per cent, the reaction was positive and in 9 of these it was strongly positive. This was about the same reactivity that we found in our control group. The time after onset seemed to have no relation to the presence of cutaneous reactivity or to the intensity of the reaction, if present. Of the 9 strongly positive reactions, 7 were definitely associated with recent acute infection or rheumatism; of the 9 negative reactions, 4 were

associated with recent acute infection. Since the group was small and the evidence for scarlet fever was taken from the history, one must be cautious in interpreting the results. The data seem to indicate that the majority of children who have had scarlet fever retain a reactivity of the skin to the nucleoproteins for a number of years and that the more intense reactions are associated with recent acute infection.

Gibson and McGibbon,[8] using an extract of scarlatinal streptococci prepared without chemical treatment of the organisms, tested 28 patients with scarlet fever. The age group was from 1½ to 24 years. These workers did not encounter a positive reaction in the first week of the disease; 22 of the 28 patients gave a positive reaction during the second to the fourth week after the onset. The authors thought that age must have been a factor in accounting for the reaction's remaining negative in



Cutaneous reactions to hemolytic streptococcus nucleoprotein K (Heidelberger and Kendall) in a control group of 617 children who did not have scarlet fever, rheumatic fever or nephritis. The solid black area indicates a definitely positive reaction and the shaded area, a strong reaction.

6 cases; these occurred in children under 7 years of age. There were 9 other children in the same age group who did give a positive reaction. In this connection it is pertinent to note that the youngest child in our group, 20 months of age, who gave a negative reaction in the first week, showed a strongly positive reaction in the second week, and in the third, fourth and fifth week of the disease still showed a + + + + reaction to only one-half the skin test dose. Gibson and McGibbon concluded that infection with hemolytic streptococci induces a condition of hypersensitiveness to intracellular products of the organism and that this allergic condition arises de novo and does not represent the return of a previously reactive state which has been suppressed temporarily by fever.

Somewhat later McGibbon [5] tested 74 patients with scarlet fever. He found that all patients gave a negative reaction at the onset, that in 8 (chiefly younger children from 1 to 5 years) the reaction remained negative throughout the period of observation and that in the remaining 66 the reaction became positive. In this paper he reaffirmed his belief in the immediate relationship between infection with scarlet fever and the subsequently positive cutaneous reaction and cited as evidence against the possibility that fever may temporarily inhibit a previously positive reaction the fact, which he demonstrated, that patients do exhibit a positive reaction during the acute stages of erysipelas. The implication from the data and conclusions of Gibson and McGibbon is that all patients give a negative cutaneous reaction to nucleoprotein prior to the time they have scarlet fever. From a study of the results in our control group (chart) we would expect at least 50 per cent cutaneous reactivity to nucleoprotein in the age group studied by Gibson and McGibbon and in our series. Furthermore, it has been shown by Swift, Wilson and Todd,[6] MacKenzie and Hanger [7] and Coburn [8] that the majority of patients with rheumatic fever give a positive cutaneous reaction to nucleoprotein. Hansen-Pruss, Longcope and O'Brien [9] found that the great majority of patients with acute glomerulonephritis have a cutaneous sensitivity to products of hemolytic streptococci. In our control group and in the patients with rheumatic fever and nephritis the number of children with a history of scarlatiniform rash is not significant. It would appear, therefore, that infections with hemolytic streptococci other than scarlet fever can incite cutaneous reactivity to nucleoprotein. It is fair to assume that a large proportion of the children who contracted scarlet fever had previously experienced other infections with hemolytic streptococci. Therefore, it seems unlikely to us that we would find almost 100 per cent negative cutaneous reactivity in children in the age group under discussion. The explanation of Gibson and McGibbon cannot be ignored, but we are inclined to believe that the negative cutaneous reactivity observed during the

5. McGibbon, J. P.: Cutaneous Reactions to Products of the Haemolytic Streptococcus in Scarlet Fever and Erysipelas, Lancet **2**:369, 1933.

6. Swift, H. F.; Wilson, M. G., and Todd, E. W.: Skin Reactions of Patients with Rheumatic Fever to Toxic Filtrates of Streptococcus, Am. J. Dis. Child. **37**:98 (Jan.) 1929.

7. MacKenzie, G. M., and Hanger, F. M., Jr.: Allergic Reactions to Streptococcus Antigens, J. Immunol. **13**:41, 1927.

8. Coburn, A. L.: The Factor of Infection in the Rheumatic State, Baltimore, Williams & Wilkins Company, 1931.

9. Hansen-Pruss, O. C.; Longcope, W. T., and O'Brien, D. P.: Skin Reactions to Filtrates of Haemolytic Streptococci in Acute and Subacute Nephritis, J. Clin. Investigation **7**:543, 1929.

first week of scarlet fever may depend on another factor. Derrick [10] showed that a small amount of nucleoprotein injected intravenously will in the majority of cases of nephritis diminish or abolish cutaneous reactivity to this substance. We have made the same observation. It is conceivable that many children who have scarlet fever were previously sensitive to the nucleoprotein but that at the onset of infection enough antigen was absorbed by the organism to abolish cutaneous reactivity temporarily.

RELATION OF THE CUTANEOUS REACTION TO URINARY FINDINGS

Studies published in 1933 [11] showed that children with scarlet fever exhibit a slight transient increase in the excretion of protein and formed elements in the urine from two to four weeks after the onset. The work has been repeated and confirmed in a larger series of cases in three different years; so we may conclude that practically all patients with scarlet fever have an attack of "micronephritis" or subclinical nephritis following the disease. These flare-ups in the urine differ from true glomerulonephritis only in duration and degree.

Since it has been suggested that the development of acute glomerulonephritis is related in some way to immunologic processes following infection with hemolytic streptococci, we were interested in correlating the development of sensitivity to hemolytic streptococcus nucleoprotein with the minor inflammatory processes in the kidneys. Quantitative studies of the sediment in the urine were made on 26 patients, all of whom exhibited the usual transient abnormalities. These abnormalities occurred during the period from eight to thirty days after the onset, the same period during which sensitivity to nucleoprotein developed in the skin. However, this fact alone is obviously not sufficient to establish a causal relationship. Unfortunately, it was not possible to perform cutaneous tests frequently enough to demonstrate a close time relationship between the factors. Several features, however, suggest that the relationship is not one of cause and effect. It will be recalled that in general the presence of complications aggravates the intensity of both the cutaneous test and the urinary reaction. However, among 8 children who did not have complications but in whom the dermal reaction was intense the urinary changes remained moderate. The fact is suggested that both the cutaneous reaction and renal irritation are more closely related to the infectious process than they are to each other. Moreover, 1 patient in whom true nephritis developed

10. Derrick, C. L., and O'Hare, J. P.: Treatment of Subacute Hemorrhagic Nephritis with Streptococcus Vaccines, New England J. Med. **208**:578, 1933.

11. Lyttle, J. D.: The Addis Sediment Count in Scarlet Fever, J. Clin. Investigation **12**:95, 1933.

did not react differently from many others in whom the urinary changes were mild. This patient was a boy of 12 in whom mild glomerulonephritis developed on the twenty-first day of the disease, accompanied by an exacerbation of tonsillitis and cervical adenitis. His cutaneous reaction was negative on the fifth day and strongly positive (+++) on the thirteenth day; on the twentieth day and subsequently it was ++++. These reactions were exactly like those of a younger child in whom sinusitis and cervical adenitis developed on the fourteenth day of the disease, with no more than the usual urinary changes.

In another series of cases of acute glomerulonephritis following infection of the upper respiratory tract cutaneous reactions to hemolytic streptococcus nucleoprotein were practically 100 per cent positive. These were similar to the reactions in cases of infection with hemolytic streptococci without nephritis, and there was nothing unusual about the severity or persistence of the cutaneous reaction.

Six hundred and seventeen children from 2 months to 13 years old in the wards of the Babies Hospital were used as a control group. They were a varied group from the diagnostic standpoint, except that the group did not include cases of scarlet fever, rheumatic fever or nephritis. Tests were made from November to July over a period of three years. The results are shown in the chart, which shows (1) how reactivity increases with age and (2) how few strong reactions there are in children under the age of 6. This finding is in accord with the work of numerous other investigators who have reported a low proportion of young children exhibiting dermal reactivity to streptococcic products. However, most of these studies are not strictly comparable with ours, as filtrates rather than cell protein were used in performing the tests.

Our data can be compared to those of Ando and Ozaki [2] and to those of Derrick and Fulton.[1] Ando and Ozaki reported that of 96 children from 2 to 5 years of age tested with scarlatinal streptococcus nucleoprotein, 14.6 per cent gave a positive reaction; of 289 children aged from 6 to 10, 41.5 per cent gave a positive reaction and of 199 children aged from 11 to 15, 56.8 per cent gave a positive reaction. Derrick and Fulton gave the following figures on a control group of children up to 15 years:

Age, Years	Number of Cases	Reaction			Negative, Percentage
		0 to ±	+ to ++	+++ to ++++	
0 to 5	60	58	2	0	96.6
6 to 10	23	20	3	0	87.0
11 to 15	23	15	4	4	65.0

Our results show that in a miscellaneous group of children who did not have scarlet fever, rheumatism or nephritis, 14 per cent in the first year of life were sensitive cutaneously to streptococcus nucleo-

protein. The proportion of children with cutaneous sensitivity increases with age until after 7 years, when 77 per cent give a positive reaction. Below the age of 7, children with a strong reaction are rarely encountered —less than 2 per cent in this series. Our data indicate that a larger percentage of young children are capable of giving a reaction than has been previously reported. Differences in the reported observations may be due to season, locality or the material used for testing.

SUMMARY

Cutaneous reactivity to hemolytic streptococcus nucleoproteins has been studied in a group of children with scarlet fever and in a control group.

The majority of children with scarlet fever give a negative cutaneous reaction to the nucleoprotein in the first week of the disease, which becomes positive after the second week. Those children who have complications usually have a strongly positive reaction. Of 20 children tested from two to nine months after the onset of scarlet fever all gave a positive reaction. Possible explanations for these changes have been discussed.

One patient with scarlet fever in whom nephritis developed showed the same changes in cutaneous reactivity as were seen in the other patients who did not have nephritis. Quantitative studies of the urine in 26 other patients showed that minor inflammatory processes were going on in the kidneys during the period when cutaneous sensitivity was developing, but the relationship could not be shown to be one of cause and effect.

A large percentage of children who have not had rheumatic fever, nephritis or scarlet fever have a cutaneous sensitivity to hemolytic streptococcus nucleoproteins. Strongly positive reactions are rarely observed below the age of 7.

PROPHYLACTIC USE OF PARENTS' WHOLE BLOOD IN ANTERIOR POLIOMYELITIS

PHILADELPHIA EPIDEMIC OF 1932

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The great need for the prevention of poliomyelitis prompted this study of the effects of parents' whole blood and convalescent serum used solely as a prophylactic measure. Poliomeylitis developed in a certain number of children who received the injections. We have attempted to correlate the potency of the blood of the donors with the type of disease experienced by the children and to compare the potency of the donor's blood with that of the blood of the children when they became convalescent. Finally, we determined the immune properties of the blood of physicians and a nurse who had been in attendance on patients with poliomyelitis.

Passive immunization to anterior poliomyelitis by means of adult whole blood and serum or by means of convalescent serum is based on three main premises: 1. Other virus diseases, such as measles, can be prevented or modified by similar passive immunization. 2. Several investigators have shown that it is possible thus to immunize monkeys so that they resist the later intranasal instillation or even intracerebral inoculations of the virus of poliomyelitis.[1] 3. By means of neutralization tests many workers have demonstrated the presence of immune or neutralizing bodies in the blood serum of convalescent patients and of most normal adults and in the serum of immunized or "hyperimmunized" monkeys.

It was thought by earlier investigators that convalescent serum possesses greater neutralizing power than pooled adult serum, but in recent years experiments have suggested that such is not the case.[2]

From the Department of Pediatrics, University of Pennsylvania School of Medicine and the Children's Hospital.

1. Flexner, S., and Stewart, F. W.: New England J. Med. **199**:213, 1928. Amoss, H. L., and Taylor, E.: J. Exper. Med. **25**:507, 1917.

2. Shaughnessy, H. J.; Harmon, P. H., and Gordon, F. B.: J. Prev. Med. **4**:463, 1930.

Some recent workers have even contended that as a rule the opposite is true. Whatever may be the truth of this contention it has become obvious that pooled adult serum is of great value experimentally in the passive immunization of monkeys and in neutralization tests.

It has been suggested that such a high antibody titer in pooled adult serum is due to the occurrence of subclinical types of poliomyelitis in the majority of persons during a large epidemic.[3]

Jungeblut has recently added some interesting data concerning the development of immunity in young monkeys by the injection of extract of the anterior lobe of the pituitary gland.[4] He suggested an influence of the internal secretions, particularly those concerned with sexual maturity, on the development of antibodies against the disease.

However, were it not for the apparent neutralizing properties of pooled adult serum any attempt at widespread passive immunization of children during an epidemic would be limited to the small amount of serum available from convalescent patients.

There are certain limitations to the use of pooled adult serum: 1. The expense of obtaining large quantities of serum is considerable because of the payment of donors and the cost of the Wassermann or Kahn tests and the apparatus required. 2. Time is consumed in obtaining pooled adult serum. Usually it is not stored in large quantities in preparation for an epidemic owing to the rapid diminution in antibody titer during storage.

The latter problem appears to be in the process of solution, with the recent development of improved methods of preserving serums.[5] "Lyophile" serums, desiccated by vacuum distillation from the frozen state and preserved in vacuo, are dry, sterile, readily soluble in water and have maintained their antibody titer intact for many months under the usual conditions of storage. We hope that it will be possible to maintain large quantities of such lyophile serums, selected according to their neutralizing properties against fresh virus of human poliomyelitis and available at any time to test the value of passive immunization during an epidemic of the disease.

The use of whole blood from a single parent or preferably from both parents, injected intramuscularly for passive immunization, has certain advantages: 1. It is an inexpensive procedure. 2. It saves time, since the serum is not separated. 3. The parent and the child are usually available at the same time and place. 4. Wassermann tests

3. Paul, J. R., and Trask, J. D.: J. Exper. Med. **65**:319, 1932.

4. Jungeblut, C. W., and Engle, E. T.: Susceptibility Problems in Poliomyelitis, Am. J. Dis. Child. **43**:523 (Feb.) 1932.

5. Mudd, S.; Reichel, J.; Flosdorf, E. W., and Eagle, H.: J. Immunol. **26**: 341, 1934. Stokes, J., Jr.; Mudd, S.; Flosdorf, E. W.; Eagle, H.; Lucchesi, P., and Roddy, R.: Proc. Soc. Pediat. Research, to be published.

at times may be omitted, but only with full explanation and with the consent of the parents and only in cases in which the physician has no doubt about the absence of syphilis. 5. No preservation is needed. 6. There is no loss of antibodies.

The method has also certain disadvantages: 1. Local reactions are more common, particularly those resembling the Arthus phenomenon, which occur from four to ten days following the intramuscular injection. Some immediate reactions also occur. 2. It is difficult to obtain blood of both parents when large groups of children are being given injections in outpatient clinics, and with the blood of only one parent the possibility of the injection of blood of low antibody titer is increased. This possibility is present even when the blood of both parents is used. 3. The injection is more painful than that of serum, since in comparison approximately twice the volume of fluid must be injected. 4. The possibility that the area into which injections are being made may become infected is perhaps slightly greater than that with prepared serum which has been checked bacteriologically before being used. 5. Certain diseases, such as syphilis, malaria and trypanosomiasis can be directly transmitted.

If one assumes that parents' whole blood usually contains as large amounts of immune bodies against poliomyelitis as does pooled adult serum the advantage of a readily available supply for immediate use probably will determine its choice. This procedure is particularly applicable in a community suddenly aroused to the presence of a widespread epidemic without adequate preparation for it. If in the future passive immunization with serum or whole blood proves to be effectual it is possible that the availability of lyophile serums may rectify such lack of preparation.

PROPHYLAXIS DURING THE PHILADELPHIA EPIDEMIC OF 1932

Previous to August 1932, as far as we are aware, no widespread passive immunization in the presence of an epidemic of poliomyelitis had been attempted. Such immunization had been suggested by Flexner and Stewart.[1] Davide in northern Sweden made probably the first attempt,[6] giving injections of convalescent serum to 157 persons in a small village. W. H. Park in the New York epidemic of 1931 injected from 25 to 30 cc. of convalescent serum or from 50 to 60 cc. of whole blood from parents[7] into 200 children exposed by contact. The disease developed in 2 of the children five days after the injection. In neither Davide's nor Park's small group was it possible to draw any conclusions regarding the value of such injections.

6. Davide, H.: Bull. Office internat. d'hyg. pub. **20**:74, 1928.
7. Park, W. H.: Personal communication to the authors.

For these reasons widespread passive immunization with parents' whole blood was attempted as the disease reached epidemic proportions in Philadelphia in August 1932. For a general analysis of this epidemic the reader is referred to the report of Henry and Johnson.[8]

It was decided to use 60 cc. of citrated whole blood from one parent by intramuscular injection, as this was the largest quantity of blood which could be conveniently given. We should have preferred the mixed whole blood of both parents, but since the injections were given outside the home it was impossible for both parents to be present in most cases, and we preferred a uniformity of technic.

A special temporary clinic was organized in the department for the prevention of disease of the Children's Hospital, with a large staff of nurses, physicians and social service workers. Newspaper publicity,

TABLE 1.—*Dates of Injection and the Number of Children Given an Injection on Each Date at the Children's Hospital* *

August 1932		September 1932				October 1932	
Date	Number Given Injection	Date	Number Given Injection	Date	Number Given Injection	Date	Number Given Injection
20	16	1	95	14	32	3	6
22	11	2	137	15	25		
23	12	3	61	16	11		
24	36	5	96	17	27		
25	39	6	100	19	16		
26	38	7	107	20	15		
27	38	8	64	21	4		
29	43	9	44	22	14		
30	59	10	55	23	9		
31	54	12	43	26	11		
		13	22				

* The record of one child has been omitted.

the cooperation of the Philadelphia Department of Public Health and the activity of our department for the prevention of disease brought parents and children to the clinic in large numbers from the first day it was opened. A little less than one fourth of all the cases of the epidemic had been reported to the Department of Public Health previous to the time the first injections were made on August 20. Injections were given until September 26 (table 1) and averaged forty-three daily. Each parent was questioned as to the presence of syphilis and was asked to sign a permission blank. By the use of large syringes into which 2 cc. of a 10 per cent solution of sodium citrate was first drawn it was possible to withdraw 60 cc. of donor's blood in a single maneuver. This was immediately injected into the child's buttocks, 30 cc. in each side. The entire procedure took less than five minutes. Within fifteen minutes thereafter the child was able to walk, although

8. Henry, J. N., and Johnson, G. E.: Acute Anterior Poliomyelits in Philadelphia, J. A. M. A. **103**:94 (July 14) 1934.

with some degree of pain for the next few hours. The child was kept under observation for an hour. No immediate general reactions and no local infections were observed. During the series of injections two needles broke off in the buttocks and had to be removed surgically. The only other accident was the appearance of malaria some weeks later in a brother and sister whose mother, acting as the donor, later recalled that as a child in Greece she had chills and fever for some time. No child contracted syphilis so far as we have been able to learn. In one other child multiple abscesses developed beneath the skin within a week after the injection, but there was no evidence of infection in the gluteal regions, and we are inclined to believe that the multiple abscesses were independent of the injections of blood. It was interesting to note in the follow-up period that many parents said that their children seemed more energetic and had an improved appetite for some time following the injection. These, of course, may have been entirely subjective responses.

Our social service workers made personal visits to the home of 1,341 children from one to two months later for the purpose of obtaining accurate information regarding their condition.

Of the children given injections at the Children's Hospital, approximately 27 per cent were Negro and 73 per cent were white; 49 per cent were boys and 51 per cent, girls. The distribution according to age was as follows:

Age, Years	Percentage
0 to 1	0.2
1 to 2	11.5
2 to 3	12.2
3 to 4	12.0
4 to 5	11.1
5 to 6	12.0
6 to 7	10.0
7 to 8	9.1
8 to 9	8.5
9 to 10	7.1
10 to 11	5.1
11 to 14	1.0

Table 1 shows the number and dates of injections made at the Children's Hospital in the department for the prevention of disease.

Census tracts, outlined by the Bell Telephone Company around the Children's Hospital, offered accurate statistics concerning this area of the city where the incidence of the disease was highest. Although 1,341 infants and children under 11 years of age (except about 1 per cent, or 13 children, who were between 10 and 15 years of age) received injections at the Children's Hospital, only 620 of them fell within the census tracts chosen. These tracts included a population of 23,790

under 11 years of age in 1930. Statisticians stated that the population had decreased a little since that time owing to removals. The general incidence of the disease in this area and the date of onset of each case were obtained from the spot map of the Department of Public Health and no cases were included in our comparisons of morbidity among the children who did and those who did not receive injections except those in which the disease developed following August 20. Since injections were given over the period of six weeks, the comparison between the group of children who received injections and the control group, which comprised the population in the census tract under 11 years of age that did not receive injections, could not be entirely accurate. On the other hand, we learned of several cases which occurred in the group that did not receive injections comprising the rest of the population under 11 years of age, which were never reported to the Department of

TABLE 2.—*Data on Attempted Passive Immunization*

	Age Group, Years	Number	Cubic Centimeters Injected	Poliomyelitis	Incidence‡
Children's Hospital					
Within census tracts	1 to 10*	620	60 (A.B.)†	3	1:207
Outside census tracts	1 to 10*	721	60 (A.B.)	3	1:240
Jewish Hospital	1 to 15	266	20 to 40 (A.S.)	0	0
Mount Sinai Hospital	1 to 15	229	30 (A.B.)	0	0
St. Luke's Hospital	1 to 15	343	20 (C.S.)	0	0
Total		2,179		6	1:363

* About 1 per cent, or 13, of the group of 1,341 children seen at the Children's Hospital ranged from 11 to 15 years of age.

† A.B. means adult blood; A.S., adult serum, and C.S., convalescent serum.

‡ Five hundred and twenty-one cases in children under 11 years of age of an estimated population of 289,455 in this age group gives the general incidence of the city of 1:555.

Public Health. In addition, certain children were brought to the clinic because of close contact with the disease. For these reasons we consider the comparison to be of great interest, although of less statistical value than we had hoped. However, we have tabulated the incidence of the disease both within and without the census tract and in table 2 have added the statistics furnished us by the Jewish, Mount Sinai and St. Luke's Hospital. Since no effort was made by these hospitals to confine their cases within a specified area of the city and since their groups were comparatively small, their figures are of less value from the statistical standpoint than those of the Children's Hospital. Nevertheless, table 2 is of interest as a demonstration of the difficulty of obtaining data of value for a disease of such low morbidity as poliomyelitis. This is particularly evident when one considers that in the most severe epidemics the recorded incidence has not exceeded 4 cases per thousand of population.

However, the effort expended in this attempt at widespread passive immunization was of possible value for two reasons: 1. A consider-

able number of children were brought in for injection because they had been in close contact with persons who had the disease. This may have protected a number of children from contracting poliomyelitis, although at the same time it tended to vitiate our statistical analysis. As will be demonstrated, the disease was unusually mild when contracted following the injection of whole blood. 2. The procedure of widespread passive immunization was adopted by a number of other hospitals and by many family physicians following our lead, and this gave us the opportunity to collect and study observations on a group of children who contracted the disease following the injection of whole blood or serum.

TABLE 3.—*Cases of Poliomyelitis in Which Intramuscular Injection of Whole Blood or Serum Antedated the Onset by an Interval Ordinarily Considered Adequate or Nearly Adequate* *

Patient	Age, Years	Whole Blood, Cc.	Interval Between Injection and Onset, Days	Interval Between Contact and Injection, Days	Paralysis or Weakness During Acute Attack	Spinal Fluid Cell Count	Present Status
1. W. T.	5	60	10	.....	0	620	Normal
2. A. T.	3	60	10	.....	0	280	Normal
3. J. K.	3	8†	9	.....	Paralysis of left leg	318	Residual weakness
4. A. B.	6	50	15	.....	Paralysis of both legs	119	Residual paralysis
5. R. T.	7	15†	5	.....	0	100	Normal
6. E. B.	7	60	7	3	0	180	Normal
7. M. K.	2	60	10	.....	Slight weakness of left leg	7	Normal
8. L. S.	4	60	6	13	Slight weakness of left leg	2	Normal
9. C. S.	3	50	18	Contact on day of injection	0	250	Normal
10. J. G.	6	60	8	.....	0	37	Normal
11. C. C.	6	60	6	5	0	20	Normal

* Since the incubation period of poliomyelitis is usually slightly shorter that that of measles, an analogy is useful but cannot be entirely accurate.

Before the final preparation of this paper, a careful check-up was made of those cases originally reported by us[9] and later by Henry and Johnson.[8] As a result of this check-up certain changes were made in the data both in their report and in ours, which made it necessary to alter the table somewhat. These changes are recorded in tables 3 and 4.

† Convalescent serum.

POLIOMYELITIS AFTER THE INJECTION OF ADULT WHOLE BLOOD OR SERUM

In table 3 are arranged the important data concerning 11 children in whom the injection of blood or serum antedated the onset of the disease by an interval ordinarily considered adequate or nearly adequate for protection in other virus diseases, such as measles. Since the incubation period of poliomyelitis is usually slightly shorter than that of measles, the analogy is useful but cannot be entirely accurate. The range in age was from 3 to 9 years. In 2 instances convalescent serum was given; 1 of these 2 children received but 8 cc. of mixed convalescent serum, while the other received 15 cc. of convalescent serum from a single donor. In all the other children 60 cc. of whole blood from a

single adult donor was injected, except for patients 4 and 9, who received only 50 cc. Six of the group received the blood at the Children's Hospital.

The interval between the time of injection and the onset of the first distinguishable clinical symptoms ranged from five to eighteen days. In 4 cases the onset occurred in less than eight days from the time of injection, which may have been given too late in the incubation period. Although a history of close contact with persons with the disease could be obtained for only 4 children, nevertheless in several instances not recorded there was a history of suspicious contacts. The 2 children with a very low cell count of the spinal fluid (patients 7 and 8) showed slight but definite weakness of the left leg, which confirmed the diagnosis. Otherwise, the cell count of the spinal fluid was elevated and, when considered in conjunction with the typical signs and symptoms, appeared to have diagnostic significance.

However, for 2 children (patients 10 and 11), with a cell count of the spinal fluid of 37 and 20, respectively, other diagnostic criteria should be mentioned. In case 10, 60 cc. of whole blood from the father was given intramuscularly on August 29, and on September 6 fever developed, with drowsiness, marked headache, stiff neck and hyperesthesia. There was a typical stiffness in the back, and the patient was admitted immediately to the Children's Hospital, where lumbar puncture was performed. The fever and signs gradually disappeared without evidences of weakness or paralysis.

The patient in case 11 from August 16 to 18 was exposed to a typical case of the disease in her brother, J. C. She was given 60 cc. of whole blood from her mother intramuscularly on August 23. On August 29 she complained of abdominal pain and anorexia, which were soon followed by fever, stiff neck and headache. She was admitted to the Children's Hospital, where lumbar puncture was performed, and the diagnosis was established. Weakness and paralysis did not develop.

An important finding in these 11 children was the absence in the entire group of any residual paralysis after subsidence of the acute stage, with the single exception of patient 4. In this instance the blood of the donor, drawn a few months later, proved to be inferior in neutralizing power to the blood of other adult donors drawn at the same time, as is shown in table 5. This we feel may explain the greater severity of the illness in this child. One of the children (patient 3) in the acute stage of the disease had partial paralysis of the left leg, but only a slight weakness remained after disappearance of the acute signs and symptoms. In this child the lack of protection or greater severity of the symptoms may have been due to the injection of only 8 cc. of mixed convalescent serum. We had no opportunity to study the neutralizing properties of this serum. Slight weakness of

the left leg was also present in patients 7 and 8 during the active stage, but rapidly disappeared coincidently with the disappearance of fever and the meningeal signs.

In table 4 are given the records of 4 children who should not be included among the 11 children whose cases were recorded in table 3 because on careful check-up it was found that they had received injections of blood or serum which perhaps could not be considered prophylactic for the following reasons:

E. S. had an elevated temperature at the time of the injection of whole blood, and from that time further typical signs and symptoms of the disease developed. He had no weakness or paralysis.

The record of W. R. was included among the children of table 3 in our statistical report presented before the American Pediatric

TABLE 4.—*Cases of Poliomyelitis with Very Short Interval Between the Time of Injection and the Onset of the Acute Stage or with a Long Interval in Consideration of the Small Amount of Serum Injected*

Patient	Age, Years	Whole Blood, Cc.*	Interval Between Injection and Onset, Days	Interval Between Contact and Injection, Days	Paralysis During Acute Stage	Spinal Fluid Cell Count	Present Status
E. S.	6	60	As fever started	6 to 7	0	170	Normal
W. R.	9	60	2 or less	.....	Left leg	141	Left leg paralyzed
W. McK.	8	80	3 or less	7	Bulbar, with general involvement	3	Marked general paralysis
R. H.	5	10†	23	....	0	250	Normal

* The blood was injected intramuscularly.
† Convalescent serum.

Society in May 1933.[9] At that time we thought that he had received 60 cc. of whole blood eleven days prior to the first clinical evidences of the disease, but on further investigation we found that we had been misinformed and that the whole blood was injected practically at the time of onset of the disease. As paralysis of the left leg with residual weakness developed following the attack, it was important to establish this fact.

W. McK. also received an injection of 80 cc. of whole blood almost at the time of onset of the disease. Neither W. R. nor W. McK. seemed well at the time the injection was given, although no well recognized symptoms of poliomyelitis had developed.

R. H. received an injection of convalescent serum about twenty-three days before the onset of poliomyelitis. However, we believe that

9. Stokes, J., Jr.; Wolman, I. J., and Carpenter, H. C..: The Evaluation of Parent's Whole Blood as a Prophylactic Measure in Anterior Poliomyelitis, Am. J. Dis. Child. **46**:681 (Sept.) 1933.

the small amount of serum (10 cc.) might be considered inadequate for prophylaxis when the interval between the injection and the onset was about twenty-three days. No weakness or paralysis developed, and it is possible that future evidence concerning prophylaxis in this disease might warrant a classification of the case in table 3.

NEUTRALIZATION TESTS OF THE SERUMS OF DONORS [10] AND CONVALESCENT CHILDREN

It was considered desirable to determine so far as possible the potency of the serum of donors and convalescent children.

TABLE 5.—*Neutralization Tests on the Serum of Convalescent Children and Their Donors*

Patient	Donor	Blood or Serum	Present Status	Neutralization Tests*	
				Donor's Serum	Patient's Serum
W. T.	Father	Whole blood	Normal	5.0%-plus†	5.0%-0
A. T.	Father	Whole blood	Normal	5.0%-plus	5.0%-0
A. B.	Father	Whole blood	Residual paralysis	2.0%-0 0.2%-plus	0.1%-plus
R. T.	Friend (convalescent)	Serum	Normal	5.0%-0 2.0%-0 0.2%-plus	
E. B.	Mother	Whole blood	Normal	5.0%-plus	5.0%-plus
M. K.	Mother	Whole blood	Normal	2.0%-plus	2.0%-plus
L. S.	Mother	Whole blood	Normal	5.0%-plus	2.0%-0 0.1%-plus
C. S.	Friend	Whole blood	Normal	2.0%-plus	
J. G.	Father	Whole blood	Normal	5.0%-0	
C. C.	Mother	Whole blood	Normal	2.0%-plus 0.2%-plus	0.2%-plus
W. R.	Mother	Whole blood	Residual paralysis of left leg	5.0%-0 2.0%-0 0.2%-plus	

* In all the neutralization tests 1 cc. of serum was mixed with 1 cc. of virus suspension, kept at 37 C. for two hours and then permitted to stand at icebox temperature over night before it was injected.

† Plus means neutralization of virus; 0, no neutralization of virus, and %, the percentage of suspension of the virus.

In all the neutralization tests the virus of the Philadelphia 1932 epidemic was used after three passages through monkeys at the Rockefeller Institute. Dr. Simon Flexner made this virus available. From eight to eleven months after the acute illness the blood of the donor and the recipient were withdrawn and tested at about the same time. It was more difficult to obtain blood for testing from the children than from the donors. Also, we could not always obtain a sufficient quantity of blood for the number of tests desired. A summary of the neutralization tests on the serum of many of the children with poliomyelitis and on the serum of most of their donors is given in table 5.

10. The expenses for the monkeys were defrayed by a gift from the board of managers of the Children's Hospital.

Of the 11 cases mentioned, the patient in case 4 was the only child with residual paralysis, and for this reason the neutralization tests on his donor's serum assume particular importance. Serum of the father, the donor, was tested about nine months after he had given the whole blood to his son, and it was found that the serum neutralized an equal quantity of a 0.2 per cent suspension of the virus but failed to neutralize a 2 per cent suspension of the virus. This evidence suggested a lower

TABLE 6.—*Results of Neutralization Tests on the Serum of Physicians and a Nurse*

Name	Virus Suspension, Percentage	Result in Monkeys*
I. W.	5.0	0
	0.2	Plus
	0.1	Plus
J. S.	5.0	0 (left arm paralyzed)
	0.2	Plus
J. T.	5.0	0
P. L.	5.0	Plus
I. S.	5.0	0 (paralysis of arm and legs)
	0.2	Plus
V. S.	5.0	0 (paralysis of leg)
	0.2	Plus
W. S.	5.0	0 (generalized paralysis)
J. M.	5.0	Plus
	0.1	Plus
C. S.	5.0	Plus
A. B.	5.0	0
	0.1	Plus
M. R.	5.0	0
	0.2	Plus
	0.1	Plus
S. G.	5.0	0
M. I. R.	5.0	Plus
H. H.	5.0	Plus
B. A.†	5.0	0
	0.2	Plus
L. L.	5.0	Plus
J. McK.M.	5.0	0
A. W.	5.0	Plus
C. T.	2.0	0
	0.2	Plus
C. C.	2.0	0
	0.2	Plus

* Plus indicates neutralization and 0, no neutralization.
† This physician had an attack of poliomyelitis twenty-five years previously, with residual paralysis and atrophy of the muscles of the shoulder girdle.

neutralizing power than that of the serum of a majority of the donors recorded in table 5.

In 3 instances the donor's serum showed greater neutralizing power than the serum of the convalescent child to whom the donor had given his blood. Also, it was of interest that the blood of the donor of patient 5 who had typical paralysis resulting from an attack of the disease many years previously showed comparatively low neutralizing power. These findings again raise the question as to whether convalescent

patients are adequate donors. Our evidence does not favor the use of convalescent serum as a prophylactic measure, as contrasted with adult whole blood or pooled adult serum.

In 2 instances the neutralizing power of the child's serum was excellent as compared with that of the donor. In 6 instances the donor's serum neutralized from 2 to 5 per cent suspensions of the virus, thus showing good neutralizing power, while in the serum of 3 other donors only moderate neutralizing power was noted, since the serum failed to neutralize the virus until a 0.2 per cent suspension was used.

It is possible that a donor's serum after a large epidemic contains more neutralizing properties than that of the average adult who has not passed through an epidemic, in which circumstance one would also expect to find an equally potent serum among the convalescent children. This was not true in 3 instances.

An additional study was made of the neutralizing properties of serums from interns, practicing physicians and a nurse who had been in intimate contact with a large number of cases of poliomyelitis at the time of the epidemic. We felt that this might give us comparative data concerning their serum in relation to the serum of the adult donors and of the convalescent children. A summary of these findings is given in table 6. The tests were performed at approximately the same time following the epidemic as those carried out on the serum of donors and convalescent children. The serum of only 7 of the 20 persons tested neutralized a 5 per cent suspension of the virus. On the other hand, all the specimens of serums tested neutralized a 0.2 per cent suspension of the virus.

It was our impression from these data that the potency of the serum of the donors tested was equal to, if not greater than, that of the serum of the physicians and the nurse who had been in intimate contact with acute cases.

COMMENT

It is significant that in Philadelphia as a whole the percentage of paralysis occurring among the victims of the disease was about 67 during the epidemic, while the percentage of mortality was 11.5.

A recent follow-up survey by the Department of Public Health of 605 of the 644 patients still living after the epidemic has shown a residual paralysis in 248 cases.[8] If a proportionate number of deaths, namely 70, were added to all the cases surveyed, bringing the total to 675, the combined percentage of residual paralysis plus deaths would be about 47. In short, in about one-half the cases reported to the Department of Public Health the patient has either been permanently paralyzed or died of poliomyelitis during the epidemic.

Against such a record that of the group of 11 children (table 3) whom we have reported here contrasts most favorably, even though its small size does not lend itself to statistical comparison. In this group there were no deaths.

In only 1 child, patient 4, has there been residual paralysis, and in this case the donor's serum showed less neutralizing power against the Philadelphia 1932 virus than the serum of all but 1 or possibly 2 of the other donors. While temporary paralysis was noted in case 3 during the acute stage of the disease, at present there is only a slight residual weakness, and the patient received a very small amount (8 cc.) of mixed convalescent (untested) serum.

M. K. and L. S., each of whom had slight weakness of the left leg during the acute stage of the disease, rapidly recovered normal function as the fever subsided. It seems possible that attenuation of the disease may have been accomplished in both these children.

All the other children in this group had cell counts of the spinal fluid, signs and symptoms typical of the disease, yet no weakness or paralysis developed.

It is conceivable that the vigilance of the parents and physicians was greater among the children who received the injections, and for this reason mild cases were detected more readily.

However, it was our observation that the entire population of the city, whether the children in the family received injections or not, was so keenly alive to the slightest sign of illness during the epidemic that most children with a mild case were brought to a physician or a hospital. Certainly few cases of the types recorded in table 3 would have escaped close medical supervision.

In any discussion of the value of such prophylactic measures attention should be called to the widespread immunization attempted at Bradford, Pa., during the same epidemic of 1932.[11] At the suggestion of Dr. W. Brebner a large free clinic was inaugurated by the Board of Health on September 19, which was continued until October 1. Meanwhile, family physicians throughout the town had started to inject parent's blood before the free clinic was opened and they continued to give injections until October 22. The first case in this epidemic was not reported until August 25, and the last case was reported on October 17. About 1,200 children were given injections at the free clinic, and 100 more were given injections by local physicians; the children were between the ages of 6 months and 16 years. Approximately 2,500 children in this age group did not receive an injection, thus forming in a certain sense a control group. From 15 to 20 cc. of whole blood was injected into each child. Among the 1,300 children who

11. Vogel, R. G., health officer: Personal communication to the authors.

received injections the disease developed in only 1 child, without paralysis or weakness, three days after the injection, whereas 32 cases occurred among those in the same age group who did not receive injections. However, many cases had been reported before all the injections were given, and in the latter part of the epidemic the disease was extremely mild in comparison with the severity during the earlier part. Despite the fact that a comparison of the results in the group which received and that which did not receive injections could not be entirely accurate, at the same time the clinical impression undoubtedly favored the value of parents' blood as an immunizing agent in this epidemic.

We believe, in view of the experiences in Philadelphia and in Bradford and the favorable clinical impressions derived from them, that parents' whole blood should be used as a prophylactic measure whenever possible in large epidemics of poliomyelitis, both for the sake of the children and for the purpose of accumulating further statistics regarding its value. Over the period of an epidemic more than a single injection would seem advisable, since passive immunization probably does not persist for more than from four to six weeks.

We further suggest, in view of the development of lyophile human serums, which apparently retain their antibody titer, that such serums of high neutralizing value against the virus of poliomyelitis should be made available wherever epidemics arise.[12]

SUMMARY

The reasons and methods for passive immunization as a prophylactic measure against anterior poliomyelitis have been discussed.

The results of prophylactic injection of parents' blood, pooled convalescent serum and pooled adult serum in 2,179 children in Philadelphia have been tabulated and discussed. An attempt to analyze statistically the incidence of poliomyelitis in a group of 620 children who received injections in a certain census tract area of Philadelphia and its relation to the group who did not receive injections in the same area has been described.

A small group of 11 children who contracted poliomyelitis from five to eighteen days following the injection of whole blood or serum has been described. The mild nature of the attack was emphasized as apparently favoring such prophylaxis, since residual paralysis developed in only 1 child.

12. It is probable that recent developments in active immunization will relegate passive immunization to a position of secondary importance. However, both methods or a combination of both methods deserves further intensive laboratory and clinical trial.

Neutralization tests on the serum of the convalescent children and their donors have been described. The low neutralizing power of the donor's serum in the case of the only child who suffered from residual paralysis may be of some significance. A comparison of the results of neutralization tests on the serum of physicians and a nurse intimately exposed to the disease has been discussed.

In view of the favorable results in Philadelphia and Bradford, Pa., a further trial of the injection of parents' whole blood is recommended as a prophylactic measure. The possibility that human lyophile anti-poliomyelitis serum may eliminate the present limitations of parents' whole blood has been discussed.

RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

XV. DAILY ENERGY REQUIREMENTS OF NORMAL INFANTS

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Only an occasional report of twenty-four hour measurements of the energy exchange of infants is available in the literature. The published list comprises three observations by Rubner and Heubner [1] and two by Talbot [2a] on normal infants. Actual balance studies of the total energy requirements of normal infants inclusive of their needs for growth are missing from the literature. The only studies of this nature which are available are those on two premature infants reported by Rubner and Langstein in 1915.[2b] This paucity of data is undoubtedly ascribable to the many technical difficulties inherent in prolonged measurements of the respiratory metabolism of infants and in concurrent analyses of their diet and excreta. Despite these obstacles, such balance studies are imperative, since the modern systems of feeding infants are predicated in large part on an accurate knowledge of their daily energy needs.

The energy supplements which combine to make up the total exchange include: (1) the basal metabolism, or the caloric expenditure during complete repose and in the postabsorptive state in adults or, in infants, during sleep and following the ingestion of a small meal; [3] (2) the

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1. Rubner, M., and Heubner, O.: Die natürliche Ernährung eines Säuglings, Ztschr. f. Biol. **36**:1, 1898; Die künstliche Ernährung eines normalen und eines atrophischen Säuglings, ibid. **38**:315, 1899; Zur Kenntnis der natürlichen Ernährung des Säuglings, Ztschr. f. exper. Path. u. Therap. **1**:1, 1905.

2. (*a*) Talbot, F. B.: Twenty-Four-Hour Metabolism of Two Normal Infants with Special Reference to the Total Energy Requirements of Infants, Am. J. Dis. Child. **14**:25 (July) 1917. (*b*) Rubner, M., and Langstein, L.: Energie- und Stoffwechsel zweier frühgeborener Säuglinge, Arch. f. Physiol. **39**:39, 1915

3. This connotation will apply throughout the paper to the term "basal metabolism of infants."

specific dynamic action of food, or the extra heat dissipated in the processes of digestion, absorption and assimilation, the so-called "cost of digestion"; (3) the activity quota, or the added output of energy resulting from muscular exertion, and (4) the caloric loss in the excreta. The maintenance metabolism may, therefore, be defined as the algebraic sum of these several energy increments. Apart from these catabolic factors for maintenance, it is recognized that a surplus of calories is desirable in the diet to cover the anabolic fraction utilized in the building up of new tissue for growth (the growth quota). The latter quota is especially important in infancy.[4] A calorically adequate diet for infants, therefore, is one which fully covers the energy needs for maintenance and which in addition provides a surplus for growth.

This series of investigations was undertaken with a twofold purpose: (1) to determine by direct measurement the total daily energy transformations of normal infants and (2) to assess in quantitative terms the contribution of the separate energy supplements to the total exchange. This program called for twenty-four hour measurements of the respiratory metabolism of healthy infants while on various dietary regimens, simultaneous analyses of their diet and excreta and accurate records of their behavior during the periods of observation. No similar data have heretofore been assembled, and the results have proved of sufficient physiologic and clinical interest to merit a detailed report.

METHODS

A description of the calorimeter room and the adjacent metabolic ward appeared in the first two papers of this series.[5] The experimental procedures employed in this work and in studies of the water and inorganic balances of the same infants (to be reported in subsequent communications [6]) are listed as follows:

Diets.—The formulas in all except one observation consisted of varying amounts of powdered whole milk (Klim), cane sugar and water. The ingredients were weighed accurately to within 0.1 Gm. and combined, and the mixture was divided

4. It is believed by some that the caloric needs for growth are automatically fulfilled by the other energy supplements, since there is every reason to suppose that infants grow at the same rate during periods of measurement in the respiration chamber as at other times. It is, however, undoubtedly true that the velocity of gain in body weight, in terms of energy balance is directly proportional to the excess of intake of energy over output.

5. (*a*) Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: I. Basal Metabolism of Children, Am. J. Dis. Child. **31**:323 (March) 1926. (*b*) Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: II. Ketosis and the Respiratory Exchange in Children, Am. J. Dis. Child. **31**:335 (March) 1926.

6. Wheatley, M. A.; McEachern, T. H.; Levine, S. Z.; Kelly, M.D., and Marples, E.: Water Balance Studies in Normal Infants, to be published; Inorganic Balance Studies in Normal Infants, to be published.

equally in five or six bottles which were then tightly corked.[7] The difference between the initial and final weights of the bottles at the start and at the termination of the observation twenty-four hours later and the algebraic sum of the differences in weight of the individual bottles before and after each feeding afforded a twofold measure of the daily intake. The constant results obtained in the two sets of weighings served as a check on their accuracy. A preliminary period of at least three and usually more days of a uniform diet preceded the calorimetric observations.

A thoroughly mixed, pooled sample of the powdered milk was analyzed in duplicate for its protein (macro-Kjeldahl method), fat (Roese-Gottlieb method[8]) and lactose (Folin method[9]) content. The figures obtained by chemical analysis and employed in our calculations corresponded closely to the analysis submitted by the manufacturer.[10] The daily caloric intake was obtained by multiplying the grams of protein, fat and carbohydrate by the respective constants, 4.1, 9.3 and 4.1. As an added check on the caloric intake, an aliquot sample was burned in the bomb calorimeter, the calorific values secured by direct combustion and from chemical analysis[11] closely corresponding.[12]

Urine.—The construction of the calorimeter bed, described in article VI of this series,[13] made possible accurate urinary and fecal collections in male infants. The calorimeter specimens of urine passed during the twenty-four hours were collected under oil in a weighed receptacle and analyzed in duplicate for nitrogen (macro-Kjeldahl method), water and inorganic constituents. The urinary nitrogen multiplied by the customary constants, 6.25 and 26.51, afforded a measure of the protein metabolism in grams and calories, respectively, for the twenty-four hours of the observation.[14]

Feces.—The feces passed during the twenty-four hours of observations and in the preliminary periods were collected in weighed containers and sealed with adhesive tape. Each stool was weighed as soon after defecation as possible. The pooled daily specimens were analyzed for nitrogen, fat, water and inorganic constituents,[14] and the caloric content was computed with the aid of the constants

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7. All the infants were fed at four hour intervals, the feeding at 2 a. m. being omitted in all except the first observation (experiment 166). In this observation powdered whole lactic acid milk was used.

8. Association of Official Agricultural Chemists: Official and Tentative Method of Analysis Compiled by the Committee on Editing Methods of Analysis, Washington, D. C., Association of Official Agricultural Chemists, 1930, p. 217.

9. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**: 106, 1919; A System of Blood Analysis: A Simplified and Improved Method for the Determination of Sugar, ibid. **41**:367, 1920.

10. These calculations were protein, 23.9 per cent; fat, 28 per cent, and lactose, 36.6 per cent, as against the firm's figures of 26.7, 28 and 38 per cent, respectively.

11. For this comparison the constants suggested by Newburgh and his collaborators[12] were used: protein × 5.65; fat × 9.54, and carbohydrate × 4.1.

12. Newburgh, L. H.; Johnston, M. W., and Falcon-Lesses, M.: Measurement of Total Water Exchange, J. Clin. Investigation **8**:161, 1930.

13. Levine, S. Z.; Wilson, J. R.; Berliner, F., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: VI. The Specific Dynamic Action of Food in Normal Infants, Am. J. Dis. Child. **33**:722 (May) 1927.

14. The values for fecal fat and for fecal and urinary nitrogen for the days of observation always approximated the daily values for the final two days of the preliminary periods.

employed for the diet. The fecal calories were also determined directly in the bomb calorimeter in the first observation on H. S. (experiment 166). Since the calorific values obtained by direct combustion and by calculation from chemical analysis [11] were parallel, the latter method was employed to estimate the fecal calories in the remaining observations.

Respiratory Metabolism.—A closed circuit apparatus of the Benedict-Talbot type was used to measure the energy metabolism. The apparatus, technic of measurements and methods of calculation were fully described in earlier papers.[15] Three healthy infants from 4½ to 9 months of age were studied in eight observations, each of from twenty to twenty-two hours' duration. The remaining two to four hours of the day and night were spent in removing the infant from the respiration chamber, feeding him, recording the rectal temperature, reinserting him in the chamber and allowing time for the temperature and humidity to establish equilibrium. The temperature and humidity were maintained at levels approximating the external environment and ranged between 23 and 27 C. (73.4 and 80.6 F.) and between 35 and 62 per cent, respectively. Only minor fluctuations in these factors were present throughout the twenty-four hours of individual observations.

The behavior of the infants both inside and outside of the respiration chamber was observed by inspection, recorded from minute to minute throughout the twenty-four hours of each observation and partitioned into periods of sleep and wakefulness. The hours of wakefulness in turn were subdivided into periods of quiet, restlessness, crying and feeding. Experimental periods in the respiration chamber in which the infants were awake for a portion of the time were terminated only after the subject had fallen asleep and remained asleep for twenty minutes or longer in order to permit conditions in the chamber to resume a steady state. The record of behavior thus obtained by inspection is admittedly not the ideal one, but in the absence of applicable objective methods it supplies acceptable data for expanding the energy exchange of infants while asleep and while awake, as directly measured for from twenty to twenty-two hours, in terms of the total twenty-four hours of observations.

ALCOHOL CHECKS

In accordance with our custom, the accuracy of the apparatus and technic of measurements were periodically controlled by alcohol checks, the results of which are presented in table 1.

The error in oxygen consumption on which heat production is based averaged — 2.3 per cent for the five tests, the maximum error being — 4.6 per cent on Nov. 5, 1931. The respiratory quotients averaged 0.669 as against the theoretical quotient for alcohol of 0.667—a deviation of only 0.002, the maximum deviation being + 0.007, also on November 5. The alcohol flame was so regulated that the heat dissipated per unit of time was comparable to the rate of heat production of the infants. The consistent results secured in the alcohol checks may be accepted as satisfactory evidence of the reliability of the measurements.

15. Levine, S. Z., and Wilson, J. R.[5] Levine, S. Z.; Wilson, J. R.; Berliner, F., and Rivkin, H.[13]

TABLE 1.—*Alcohol Checks for Experimental Year (1931-1932)*

Date	Minutes	Alcohol, Gm.	Water			Carbon Dioxide			Oxygen			Respiratory Quotient (Theoretical, 0.667)		Calories, Theoretical
			Theoretical, Gm.	Found, Gm.	Percentage of Error	Theoretical, Gm.	Found, Gm.	Percentage of Error	Theoretical, Gm.	Found, Gm.	Percentage of Error	Found	Percentage of Error	
Oct. 26	45	2.65	3.30	3.59	.....	5.06	5.32	.....	5.52	5.85	.....	0.661	.....	.....
	60	3.56	4.44	4.16	.....	6.79	6.26	.....	7.41	6.54	.....	0.696	.....	.....
	45	2.72	3.40	3.55	.....	5.20	5.33	.....	5.68	6.02	.....	0.644	.....	.....
Total		8.93	11.14	11.20	+ 0.2	17.06	16.91	—0.9	18.61	18.41	—1.1	0.668	+0.001	63.20
Nov. 5	60	3.93	4.91	5.01	.....	7.52	7.33	.....	8.20	7.74	.....	0.689	.....	.....
	60	3.93	4.91	4.80	.....	7.52	7.20	.....	8.20	7.93	.....	0.660	.....	.....
Total		7.87	9.82	9.81	+ 0	15.04	14.53	—3.4	16.40	15.67	—4.6	0.674	+0.007	55.70
Dec. 10	60	3.56	4.44	6.45	.....	6.79	6.61	.....	7.41	7.27	.....	0.661	.....	.....
	60	3.56	4.44	6.35	.....	6.79	6.61	.....	7.41	7.27	.....	0.661	.....	.....
	60	3.56	4.44	6.34	.....	6.79	6.61	.....	7.41	7.10	.....	0.677	.....	.....
Total		10.68	13.32*	19.14*	+43.7*	20.37	19.83	—2.7	22.23	21.64	—2.7	0.666	—0.001	75.51
March 9	60	....	....	3.76	.....	....	5.54	.....	....	6.09	.....	0.662	.....	.....
	60	....	....	1.51	.....	....	5.42	.....	....	5.80	.....	0.680	.....	.....
Total		5.86	7.35*	5.27*	—28.3*	11.20	10.96	—2.1	12.21	11.90	—2.5	0.670	+0.003	41.49
March 14	75	4.43	5.56	5.58	+ 0.4	8.47	8.44	—0.4	9.24	9.23	—0.1	0.665	—0.002	31.38
Total average		37.77	26.52	26.59	+ 0.3	72.14	70.67	—2.0	78.69	76.85	—2.3	0.669	+0.002	.....

* This figure was not included in the total average. Water was found on the floor of the chamber at the end of the observation on December 10. No explanation is at hand for the negative error found in the observation made on March 9.

REPORT OF CASES

CASE 1.—H. S., a colored boy, born on April 6, 1931, was admitted to the hospital for adoption at the age of 6 months. His past history was unobtainable. Physical examination gave normal results except for the presence of a moderate grade of rickets. The Wassermann reaction and the tuberculin reaction (Mantoux test with 0.01 mg. of tuberculin) were negative. The patient was afebrile, happy and playful throughout his stay in the hospital. He was studied in the respiration chamber for twenty-two of the twenty-four hours on November 16 and again on December 4, at 7⅓ and 8 months of age, respectively. In the interim his weight had increased from 7,540 to 8,000 Gm. with a constant and presumably adequate diet (table 2).

CASE 2.—J. F., a white boy, born on March 31, 1931, was admitted for adoption on Jan. 2, 1932. He was vigorous and healthy. The Wassermann and tuberculin reactions were negative. His energy exchange was determined for twenty-two of the twenty-four hours on the seventh day of a constant and adequate diet (January 8) at the age of 9⅓ months.

CASE 3.—J. C., a colored boy, born on Sept. 9, 1931, was admitted to the hospital on Feb. 11, 1932. His past history was unobtainable, the patient being a well boarding-out infant. Examination showed a well-nourished, healthy infant with a mild infection of the upper respiratory tract complicated by bilateral catarrhal otitis media, both of which subsided prior to observations. The Wassermann and tuberculin reactions were negative. His daily energy exchange was first measured on February 19, on the sixth day of a constant and maintenance dietary regimen. Daily measurements were repeated on the fifth day of a basal diet (February 26) and again on the fifth day of a high caloric diet (March 4).

Following an interval of one and one-half months, a second series of two twenty-four hour metabolic observations were made. In the first, made on April 15, the maintenance diet of February 19 was given; in the second on April 21, the diet remained unchanged except for a marked reduction in the intake of fluids (table 2). A preliminary period of at least three days of constant diet preceded each determination. The reduction in fluid intake in the final period of observation (from 142 to 87 Gm. per kilogram of body weight per day) induced a state of relative dehydration accompanied by a temperature ranging between 101.2 and 102.8 F. An opportunity was thus afforded of studying the influence of an elevation of body temperature, uncomplicated by infection, on the daily energy exchange of this subject.

The nutritional status, diet, and behavior of the subjects for the twenty-four hours of observations both inside and outside of the respiration chamber are recorded in table 2.

The calorimetric data are recorded in table 3. The top line in each observation denotes the total energy exchange in terms of twenty-four hours expanded from actual measurements throughout from twenty and one-half to twenty-two hours in eleven to eighteen experimental periods of from one-half to five hours. The bottom line gives the results for the periods throughout which the infants slept. The latter periods numbered from five to twelve and totaled from fourteen to seventeen

TABLE 2.—*Nutritional Status, Daily Diet and Behavior of Subjects*

Subject*	Experiment	Date	Nutritional Status				Daily Diet								Partition of Behavior in Minutes‡											
																			Awake							
							Calories		Protein, Gm.				Fluid, Gm.		Total		Asleep		Total		Quiet		Restless		Crying		Feeding
			Age, Mo.	Weight, Gm.	Height, Cm.	Surface Area, Square Meters†	Total	Per Kg.	Total	Per Kg.	Total Fat, Gm.	Total Carbohydrate, Gm.	Total	Per Kg.	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out	Out
		1931																								
H. S.	166	11/16	7⅓	7,540	70.0	0.364	809	107	34.0	4.5	40.1	72.2	1,153	153	1,299	141	1,007	6	292	135	105	...	140	..	47	..	..
H. S.	167	12/ 4	8	8,000	71.0	0.380	818	102	33.5	4.2	40.7	73.9	1,167	146	1,317	123	1,026	0	291	123	198	...	46	..	47	..	..
		1932																								
J. F.	169	1/ 8	9¼	7,290	71.0	0.366	863	118	37.2	5.1	42.0	77.8	1,123	154	1,325	115	859	0	466	115	164	77	301	8	1	0	30
J. C.	170	2/19	4½	6,350	65.0	0.326	682	107	30.0	4.7	34.1	59.1	1,092	172	1,223	217	992	1	331	216	124	112	84	49	23	17	38
J. C.	171	2/26	4¾	6,060	65.0	0.319	341	56	15.0	2.5	17.0	29.6	1,025	169	1,258	182	868	2	390	180	355	129	18	12	17	4	35
J. C.	172	3/ 4	5	6,710	65.0	0.332	863	129	37.3	5.6	43.3	75.1	986	145	1,244	196	986	3	258	193	172	98	68	52	18	4	39
J. C.	173	4/15	6½	7,390	68.0	0.356	678	92	30.2	4.1	33.7	58.9	1,046	142	1,225	215	830	6	395	209	366	150	28	25	1	6	28
J. C.	174	4/21	6¾	7,240	68.0	0.355	678	94	30.2	4.2	33.7	58.9	629	87	1,270	170	984	2	286	168	286	134	0	13	0	1	20

* All the subjects were boys.

† The surface area was estimated from the nomogram of R. R. Hannon, extended for infants and children according to the height-weight formula of Du Bois and Du Bois (Basal Metabolism in Health and Disease, ed. 2, Philadelphia, Lea & Febiger, 1927, p. 124).

‡ In this table and in table 6 "in" denotes the minutes spent within the respiration chamber; "out," the minutes spent outside the chamber.

TABLE 3.—*Calorimetric Data in Terms of Twenty-Four Hours* *

Subject	Experiment	Duration of Observation		Number of Periods	Percentage of Activity in Total Period					Average Rectal Temperature, F.	Chamber		Water, Gm.	Carbon Dioxide, Gm.	Oxygen, Gm.	Nitrogen in Urine, Gm.	Respiratory Quotient		Percentage of Nonprotein Calories from		Calories
						Awake					Average Temperature, C.	Average Humidity, per Cent					Total	Nonprotein†	Fat	Carbohydrate	
		Hrs.	Mins.		Asleep	Total	Quiet	Restless	Crying												
H. S.	166	21	39	18	78	22	8	11	3	99.4	26.2	50	302	184	153	3.7882	0.875	0.897	33.5	66.5	516
		4	52	6	...	100	36	48	16	....	....	..	389	237	197	.....	0.875	.....	....	....	664
		16	47	12	100	...	..	..	..	....	....	..	287	170	141	.....	0.877	0.898	....	....	475
H. S.	167	21	57	18	78	22	15	4	3	98.2	25.4	47	275	196	162	3.9339	0.880	0.898	33.2	66.8	548
		4	51	8	...	100	68	16	16	....	....	..	397	241	200	.....	0.877	.....	....	....	677
		17	6	10	100	...	..	..	..	....	....	..	240	183	152	.....	0.879	0.900	....	....	512
J. F.	169	22	5	15	65	35	12	23	..	98.0	24.3	62	375	200	163	4.2636	0.890	0.915	27.55	72.45	553
		7	46	6	...	100	35	65	..	....	....	..	468	242	196	.....	0.898	.....	....	....	667
		14	19	9	100	...	..	..	..	....	....	..	324	177	146	.....	0.882	0.907	....	....	493
J. C.	170	20	23	15	81	19	10	7	2	98.1	23.5	35	214	157	130	3.3967	0.884	0.906	30.5	69.5	438
		3	51	7	...	100	54	36	10	....	....	..	366	200	168	.....	0.866	.....	....	....	567
		16	32	8	100	...	..	..	..	....	....	..	182	149	122	.....	0.888	0.913	....	....	412
J. C.	171	20	58	12	69	31	28	2	1	97.5	24.0	36	184	128	115	2.2227	0.809	0.810	63.1	36.9	383
		6	20	7	...	100	91	5	4	....	....	..	229	155	142	.....	0.793	.....	....	....	472
		14	29	5	100	...	..	..	..	....	....	..	163	116	103	.....	0.818	0.821	....	....	345
J. C.	172	20	44	12	79	21	14	6	1	98.6	23.8	41	265	180	145	4.4679	0.902	0.936	20.6	79.4	493
		4	18	6	...	100	67	26	7	....	....	..	370	230	183	.....	0.913	.....	....	....	624
		16	26	6	100	...	..	..	..	....	....	..	237	167	136	.....	0.898	0.934	....	....	458
J. C.	173	20	25	13	67	33	29	3	1	98.4	24.1	36	228	173	147	3.5838	0.855	0.868	43.2	56.8	506
		6	35	6	...	100	92	8	..	....	....	..	275	212	180	.....	0.857	.....	....	....	608
		13	50	7	100	...	..	..	..	....	....	..	204	155	131	.....	0.858	0.875	....	....	441
J. C.	174	21	10	11	77	23	23	..	..	101.7	26.9	46	270	184	156	4.3219	0.856	0.872	41.8	58.2	525
		4	46	6	...	100	100	..	..	....	....	..	365	213	178	.....	0.867	.....	....	....	601
		16	24	5	100	...	..	..	..	....	....	..	243	175	148	.....	0.859	0.877	....	....	503

* In each observation the top line gives the energy exchange for the enfire time in the respiration chamber; the middle line, that for periods of wakefulness, and the bottom line, that for periods of sleep. In order to conserve space the detailed calorimetric data for the individual periods are not recorded.

† Since the specimens of urine passed during the twenty-four hours could not be collected separately during sleep and wakefulness, the nonprotein respiratory quotients for these periods are not as significant as the total quotients for each observation. For this reason the nonprotein respiratory quotients for the periods of wakefulness are not given.

hours in the different observations. The middle line presents the data for the energy exchange of the infants during the time when they were awake in the respiration chamber. The number of these periods varied from six to eight, and their duration from four to eight hours. Since the periods of wakefulness were never terminated until the infants had been asleep again for at least twenty minutes, the calories metabolized in the latter fraction of these periods as calculated from the periods in which the infants slept throughout were deducted from the total caloric output, and the values thus obtained for the metabolism per unit of time for an infant while awake were expanded to twenty-four hours.

RESULTS

An analysis will first be made of the individual components of the total energy exchange of the infants, following which their energy requirements as a whole will be reviewed.

Basal Metabolism.—Reliable standards for the basal metabolism of normal infants are available,[16] and biometric analysis has demonstrated their validity, whether they are based on body weight, stature or a combination of the two.[17] In view of their availability and reliability, the published standards afford a convenient basis for appraising accretions in metabolism attributable to the other energy supplements previously enumerated.

In all the eight observations reported in this paper except one (experiment 171) the infants received diets throughout the twenty-four hours of observations which fulfilled or exceeded the daily caloric needs so that individual meals were richer in calories than those customarily given before standard measurements for infants were made. In consequence, the data for the periods of sleep, with one exception, really represent a summation of the basal metabolism plus the cost of digestion of food and for this reason are incorporated in the following section dealing with specific dynamic action.

Specific Dynamic Action of Formulas of Cow's Milk.—The effect of food on the metabolism of the infants while asleep is recorded in table 4. The composite data were collected from seven observations of fifty-one individual periods totaling ninety-five hours.[18] The periods of sleep in

16. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Publ. 302 Carnegie Institution of Washington, 1921. Talbot, F. B.: Basal Metabolism of Children, Physiol. Rev. **5**:490, 1925.

17. Levine, S. Z., and Marples, E.: The Respiratory Metabolism in Infancy and in Childhood: XII. A Biometric Study of Basal Metabolism in Normal Infants, Am. J. Dis. Child. **41**:1332 (June) 1931.

18. Experiment 174 is not included in this analysis, since in this observation the specific dynamic action of food could not be differentiated from the stimulating effect of fever.

each observation were evenly distributed between feedings, often beginning as early as from twenty to forty minutes after the last meal and frequently terminating at the time of the succeeding meal. The data, therefore, are suitable for evaluating the stimulating effect of food throughout the day.

Table 4 is arranged in ascending fashion according to the intake of calories and protein, and the heat production of the infants is compared with their basal metabolic rates predicted from the standards based on height and weight,[17] and in the case of J. C. also on his own directly measured basal metabolic level (experiment 171). In the latter observation of fourteen and one-half hours the dietary conditions may properly be termed "basal" since the daily intake of 341 calories (56 per kilogram) which the infant was receiving practically coincided with his daily basal

TABLE 4.—*Specific Dynamic Action of Formulas of Cow's Milk*

Subject	Experiment	Duration of Observation		Daily Diet		Basal Metabolic Standard*	Calories Measured			Percentage Rise Above Basal Metabolic Rate	
		Hrs.	Mins.	Calories per Kg.	Protein, Gm. per Kg.		Total per 24 Hours	Per Kg. per 24 Hours	Per Sq. Meter per Hour		
J. C.	171	14	29	56	2.5	352	345	56.9	45.0	−2	Basal diet
J. C.	173	13	50	92	4.1	416	441	59.7	51.6	6	Maintenance diets
H. S.	167	17	6	102	4.3	456	512	64.0	56.1	12	
H. S.	166	16	47	107	4.5	437	475	63.1	54.4	9	
J. C.	170	16	32	107	4.7	362	412	64.9	52.7	14	
J. F.	169	14	19	118	5.1	438	493	67.6	56.1	13	
Average (weighted)...				108	4.6			64.5	54.5	11	
J. C.	172	16	26	129	5.6	372	458	68.3	57.5	23	High caloric diet

* The basal figures given in this column were derived from the nomogram of Levine and Marples [17] based on weight and height. They correspond closely with the values predicted from the standards of Benedict and Talbot based on either weight or height.[16]

rate of 345 calories (56.9 per kilogram), determined by direct measurement. The basal figures secured in this prolonged observation under dietary conditions comparable to those customarily employed for short estimations of the basal metabolism of infants deviate by only 2 per cent from the published basal standards and thus affirm their validity.

Five observations were made on the three infants while they were on so-called maintenance diets containing approximately 110 calories and from 4 to 5 Gm. of protein per kilogram of body weight. Diets of this type are ordinarily employed in the feeding of infants. With this normal dietary regimen the daily heat production of the three infants during sleep averaged 64.5 calories per kilogram of body weight for the five observations. A consistent relationship existed within the group between the size of diet and the level of the energy exchange, the latter rising from a minimum of 60 to a maximum of 68 calories per kilogram as the calories of the daily diet were increased from 92 to 118, and the

protein from 4.1 to 5.1 Gm., per kilogram. In terms of percentages, the increments following these maintenance meals ranged from 6 to 14 and averaged 11 per cent above the basal levels predicted for the three infants from the nomogram of Levine and Marples.[17] In the case of J. C. the percentage rise was practically the same when calculated from the predicted or the measured basal level. These percentages compare favorably with the range of from 5 to 13 per cent previously reported for the specific dynamic action of similar diets in normal infants when measured for short periods.[13]

Observations on infant J. C. were next made while he was on a high caloric level of feeding for a period of five days during which he received daily a formula of cow's milk similar to that given in the

TABLE 5.—*Effect of Wakefulness on Energy Metabolism*

Subject	Experiment	Duration of Observation		Percentage of Activity in Total Period					Respiratory Quotient	Calories per 24 Hours	Rise Above Metabolism of Sleeping Infants	
					Awake							
		Hrs.	Mins.	Asleep	Total	Quiet	Restless	Crying			Calories	Per Cent
H. S.	166	14	47	100	...	..	..	..	0.877	475	...	..
		4	52	...	100	36	48	16	0.875	664	189	40
H. S.	167	17	6	100	...	..	..	..	0.879	512	...	..
		4	51	...	100	68	16	16	0.877	677	165	32
J. F.	169	14	19	100	...	..	..	..	0.882	493	...	..
		7	46	...	100	35	65	..	0.898	667	174	35
J. C.	170	16	32	100	...	..	..	..	0.888	412	...	..
		3	51	...	100	54	36	10	0.866	567	155	38
J. C.	171	14	29	100	...	..	..	..	0.818	345	...	..
		6	29	...	100	91	5	4	0.793	472	127	37
J. C.	172	16	26	100	...	..	..	..	0.898	458	...	..
		4	18	...	100	67	26	7	0.913	624	166	36
J. C.	173	13	50	100	...	..	..	..	0.858	441	...	..
		6	35	...	100	92	8	..	0.857	608	167	38
J. C.	174	16	24	100	...	..	..	..	0.859	503	...	..
		4	46	...	100	100	..	..	0.867	601	98	19*
Average (weighted)												36

* This figure was not included in the average.

previous observations but in markedly increased amounts. His daily heat production, as measured in the respiration chamber on the sixth day of the diet during sixteen and one-half hours of sleep, had risen from a basal level of 56.9 calories (experiment 171) and from an average maintenance level of 62.3 calories (experiments 173 and 170) to the high caloric level of 68.3 calories per kilogram of body weight (experiment 172). The ingestion of high caloric feedings of cow's milk under otherwise comparable conditions stimulated the metabolism of this infant while asleep so that it reached a total of 20 per cent above the level established with a daily diet just sufficient to cover his basal metabolic needs and 10 per cent above the established level with a maintenance dietary regimen.

Effect of Wakefulness on Metabolism.—The minute to minute record of behavior kept for each infant while in the respiration chamber per-

mitted a comparison of the metabolism of the subjects while asleep and awake. The data presented in table 5 were collected from a total of sixty-two sleeping and fifty-two wakeful periods of one hundred and sixteen and forty-three and one-half hours, respectively. Since the latter periods were never terminated until the infants had fallen asleep and remained asleep for at least twenty minutes, the calories produced while asleep were deducted from the total caloric output of these periods in calculating the metabolism of the infants while awake.

The daily heat production of the infants in the waking state was from 98 to 189 calories, or from 19 to 40 per cent higher than their basal metabolism as determined for sleeping periods of the same observations. A rough parallelism was evident between the degree of activity and the metabolic increments. When the infants were quiet and free from gross muscular movements for more than 90 per cent of the wakeful periods (experiments 171, 173 and 174) their daily accretions in metabolism were 127, 167 and 98 calories, respectively, whereas in the observations associated with greater restlessness the augmentation in the output of heat tended to be higher (from 155 to 189 calories in twenty-four hours). This relation is especially clear in the last observation (experiment 174), during which the infant was extremely quiet throughout his stay in the respiration chamber with the result that a minimum of 98 extra calories was expended in the twenty-four hours. It seems futile to attempt a more precise analysis of the stimulating effect of activity in the absence of objective methods for appraising even crudely the mechanical work performed by infants in crying, eating and in the execution of various movements. It is sufficient to state that the average metabolic increment of 36 per cent found in these observations on infants while awake under experimental conditions associated with restriction of physical activity probably falls below the metabolic acceleration resulting from activity in the natural infantile environment. The average activity quota of 36 per cent obtained in these three artificially fed infants ranging in age from 4½ to 9 months is also somewhat lower than the values of 50 and 42 per cent found by Talbot [2] in two breast-fed infants of 6 and 5 months and is probably explained by greater activity in the latter infants.[19]

To estimate the energy metabolism of the infants for the total twenty-four hours, the maximum rate of energy exchange as measured in the respiration chamber during periods of wakefulness was assumed to apply for the two to three and one-half hours spent outside the chamber, and the calories thus obtained were added to those actually measured for the remainder of the twenty-four hours. As previously

19. The increases of 67 and 70 per cent appearing in the publication of Talbot are obviously errors in printing since the calories rose 143 above the basal level of 285 in the first infant and 143 above the basal rate of 338 in the second infant.

TABLE 6.—*Total Daily Energy and Intermediary Metabolism*

Subject	Experiment	Time Spent In Hrs.	Time Spent In Mins.	Time Spent Out Hrs.	Time Spent Out Mins.	Percentage of 24 Hours Awake	Calories In	Calories Out	Calories Total	Calories Per Kg. per 24 Hours	Percentage Rise Above Metabolism of Sleeping Infants	Combustion of Protein Gm.	Protein Percentage of Calories	Fat Gm.	Fat Percentage of Calories	Carbohydrate Gm.	Carbohydrate Percentage of Calories	
J. C.	171	20	58	3	2	40	335	60	395	65	14	14.4	15	22.8	54	30.2	31	Basal diet
J. C.	173	20	25	3	35	42	430	91	521	71	18	23.2	18	19.8	36	59.0	46	Maintenance diets
J. C.	174	21	10	2	50	32*	463	71	534	74*	6*	27.9	21	18.8	33	59.5	46	
J. C.	170	20	23	3	37	38	372	85	457	72	11	22.0	20	12.0	24	62.2	56	
H. S.	167	21	57	2	3	29	501	58	559	70	9	25.4	19	16.2	27	74.1	54	
H. S.	166	21	39	2	21	30	465	65	530	70	12	24.5	19	15.5	27	69.8	54	
J. F.	169	22	5	1	55	40	509	53	562	77	14	27.6	20	13.3	22	79.3	58	
J. C.	172	20	44	3	16	31	426	85	511	76	12	28.9	23	8.7	16	76.1	61	High caloric diet
Average (weighted)						36				73	14							

* This figure was not included in the average.

mentioned, the freedom from artificial restraint during the periods outside of the chamber probably resulted in more vigorous activity and in presumably greater, but with the present methods unmeasurable (owing to feeding and the taking of the rectal temperature, etc.), heat production. The results are given in table 6.

The daily heat production of the infants under conditions of limited muscular activity (awake from 30 to 40 per cent of the twenty-four hours and unusually quiet for the major portion of the waking time [table 2]) and on varied diets ranged between 65 and 76 calories per kilogram of body weight, the levels roughly corresponding to the degree of activity and to the type of diet. For example, while on the so-called basal regimen infant J. C. expended 65 calories per kilogram in twenty-four hours (experiment 171); under maintenance conditions of diet, 71.5 calories (experiments 170 and 173) and on a high caloric intake, 76 calories (experiment 172). The metabolic rate in the five observations on the three infants while they were on maintenance diets averaged 73 calories per kilogram in twenty-four hours and varied between 70 and 77 calories. These figures closely approximate the values of 74 and 70 calories reported by Talbot [2] for the daily energy metabolism of two breast-fed infants. The daily metabolism of the infants averaged 14 per cent and ranged between 6 and 18 per cent above their basal (sleeping) levels.[20]

20. It must again be emphasized that attempts to appraise accurately the effect of muscular activity on the energy metabolism of infants are open to a number of criticisms, the most important of which may briefly be listed as follows: (1) the absence of objective methods for estimating the mechanical work performed by infants in the execution of different movements; (2) the method of inspection in lieu of practical objective methods for recording behavior; (3) the artificial curtailment of activity imposed by the conditions of calorimetric observations with the present forms of apparatus; (4) the notable variation in the daily behavior of different infants in presumably good health and even of the same infant on different days under essentially similar conditions. The first two objections are, in the present state of knowledge, well nigh insurmountable. An attempt was made to overcome the latter two criticisms by recording accurately the daily behavior of the infants for the three to five days of preliminary periods under conditions more closely simulating their natural environment and, in addition, by securing accurate records of behavior over prolonged periods of a large group of infants in an essentially normal environment. The detailed data relating to these subjects will be reported in a subsequent communication.

In this connection the brief statement may be made that the three infants in sixteen days of preliminary periods remained awake from 46 to 54 per cent of the twenty-four hours as against the 30 to 40 per cent recorded for the days of observation in the respiration chamber. In the larger series of fourteen healthy infants from 4 to 9 months of age, the proportion of time the infants remained awake, as estimated from minute to minute records of behavior for a total of sixty-one days of observation, averaged 50 per cent and varied between 46 and 61 per cent of the twenty-four hours.

If the customary procedure is followed of accepting the level of the respiratory quotient as an index of the composition of the metabolic mixture, their similarity in periods of sleep and wakefulness in all the observations (table 5) may be regarded as good evidence that infants as well as children [21] and adults [22] utilize all types of foodstuffs during activity and argues against the exclusive rôle of carbohydrate as the fuel of exercise.

The qualitative constancy of metabolic mixtures in sleep and activity justified expansion of the calculation of foodstuffs metabolized by the infants for the time spent outside of the respiration chamber from their urinary nitrogen and from the levels of their nonprotein respiratory quotients while in the chamber (table 3). The proportion of total calories derived from the combustion of carbohydrate rose from 31 per cent with the basal diet (experiment 171) to 54 per cent with the maintenance diet (an average of six experiments) and to 61 per cent with the high caloric diet (experiment 172). The proportion derived from protein rose from 15 to 19 to 23 per cent, while the calories contributed by fat fell from 54 to 27 to 16 per cent with the three types of diet. The infants preferentially metabolized the carbohydrate given in the diet when it was ample to cover their energy needs. Only with a dearth of this readily combustible material in the diet (basal diet) were ingested and body fat drawn on to any great extent to meet the metabolic requirements.

Caloric Loss in Feces.—A quantitative estimate of the daily energy requirements must include, in addition to the three energy factors previously enumerated, the calories lost in the feces. This loss results from the incomplete digestion and assimilation of the organic foodstuffs, protein and fat. The carbohydrate of the infant's diet is generally assumed to be completely digested under normal conditions. If any escapes absorption it undergoes fermentation in the alimentary tract, so that no carbohydrate as such is ordinarily recovered in the feces. The caloric equivalents of the feces are given in table 7.

The fecal calories rose from 41 to 153 in twenty-four hours as the calories of the daily diet were increased from 341 to 863, but the caloric loss, with one exception (experiment 169), remained at a practically constant level of between 8 and 12 per cent of the caloric intake.

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21. Wilson, J. R.; Levine, S. Z.; Rivkin, H., and Berliner, F.: The Respiratory Metabolism in Infancy and in Childhood: V. Effect of Moderate Exercise on the Respiratory Quotient: Study of Four Children, Am. J. Dis. Child. **33**:618 (April) 1927.

22. Lusk, G.: Die Energiequelle bei der Muskelarbeit, Biochem. Ztschr. **156**: 334, 1925. Richardson, H. B., and Levine, S. Z.: Exercise and the Respiratory Quotient in Diabetes, J. Biol. Chem. **66**:161, 1925. Benedict, F. G., and Cathcart, C. P.: Muscular Work. A Metabolic Study with Especial Reference to the Efficiency of the Human Body, Publ. 187, Carnegie Instituton of Washington, 1913.

In experiment 169 the fecal calories comprised 18 per cent of the intake, the high rate of loss being referable to an excessive excretion of undigested fat (the infant had four bulky, light-colored stools on the day of observation). The proportion of dietary calories excreted in the feces in the seven other observations averaged 10 per cent, a figure in accord with the generally accepted one for loss in the excreta. This relation was maintained irrespective of the total moist weight of the stools. The fecal increment comprised from 12 to 35 per cent of the basal quota with the different diets, the average increment being 16 per cent for the five observations (experiment 169 not included) with maintenance diets.

Effect of Fever.—In addition to the four usual components of the energy exchange, it is generally recognized that the presence of fever,

TABLE 7.—*Caloric Loss in Feces*

Subject	Experiment	Diet, Calories	Basal Metabolic Rate*	Feces				Fecal Calories		
				Calories	Protein, Gm.	Fat, Gm.	Weight, Gm.†	Percentage of Diet	Percentage of Basal Metabolic Rate	
J. C.	171	341	345	41	2.5	3.3	28	12	12	Basal diet
J. C.	173	678	416	56	2.4	4.9	57	8	13	Maintenance diets
J. C.	174	678	412	51	2.0	4.7	47	8	12	
J. C.	170	682	362	54	2.6	4.7	69	8	15	
H. S.	167	818	456	85	3.4	7.6	85	10	19	
H. S.	166	809	437	86	3.7	7.6	131	11	19	
J. F.	169	863	438	153	5.0	14.2	83	18‡	35‡	
Average (weighted)								10	16	
J. C.	172	863	372	98	4.1	8.7	143	10	26	High caloric diet

* This was predicted from the basal standards [17] except in experiment 171, which was carried out under basal conditions of diet.
† The total moist weight.
‡ This figure was not included in the average.

irrespective of its origin, leads to an acceleration of the metabolic rate. In a large variety of infectious conditions in adults Du Bois and his co-workers [23] found this febrile increment to average about 13 per cent for each rise through a degree centigrade in body (rectal) temperature. To our knowledge, no figures are available for infants.

In the course of these studies a rare opportunity presented itself of appraising in quantitative terms the effect of an elevation of body (rectal) temperature, uncomplicated by infection, on the energy metabolism of one infant under carefully controlled experimental conditions. The metabolic rate of this infant was first determined on the fifth day of a maintenance diet, when he was afebrile (experiment 173). Following this control observation he continued to receive the same diet, but the fluid intake was reduced from a daily level of 142 to 87 Gm.

23. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lea & Febiger, 1924, p. 330.

per kilogram. On the third day of this low fluid regimen, when his rectal temperature had attained an average level of 101.7 F., he was again studied in the respiration chamber (experiment 174). The results obtained in the sleeping periods of fourteen and sixteen and one-half hours in these two observations under strictly comparable conditions furnish the requisite data for evaluating the stimulating effect of dehydration fever on the energy metabolism of this infant (table 8).

Coincident with, or as the result of, fever, the heat production of the infant during sleep rose from 441 to 503 calories in twenty-four hours, an augmentation of 14.1 per cent, with an average elevation in rectal temperature of 1.8 C. (3.3 F.). This febrile increment equivalent to 8 per cent per 1 degree C. is appreciably lower than the 13 per cent found by Du Bois in febrile adults suffering from various infections. This discrepancy may possibly be explained both by the absence of infection and accompanying manifestations of toxicity and by the relatively low grade of fever in our infant.[24]

TABLE 8.—*Effect of Fever on Energy Metabolism*

				Subject J. C.									
		Duration of Observation		Diet		Respiratory	Calories per 24 Hours		Percentage	Rectal Temperature, F.			Percentage
Experiment	Weight, Gm.	Hrs.	Mins.	Calories	Fluid, Gm.	Quotient	Total	Per Kg.	Rise	Average	Minimum	Maximum	Rise per 1 C.
173	7,390	13	50	678	1,046	0.855	441	59.7	....	98.4	97.2	99.4	...
174	7,240	16	24	678	629	0.856	503	69.5	14.1	101.7	101.2	102.8	7.7

The similarity of the average respiratory quotients in the observations made in the presence and the absence of fever indicates that in this infant the accelerated energy metabolism resulting from fever, as has already been shown for the increased quota from exercise, is at the expense of all three types of foodstuffs without preferential selection of carbohydrate.

Total Energy Transformations of Normal Infants in Twenty-Four Hours.—The composite data derived from prolonged and concurrent measurements of the respiratory metabolism, of the urinary nitrogen and of the caloric loss in the feces provide precise information regarding the composition of the total daily energy transformations of healthy infants under carefully controlled conditions of diet and activity. The average calories, per kilogram of body weight and in terms of percentage

24. It must be pointed out that the rectal temperature is not an absolutely reliable index of the entire body temperature, especially when the former is taken with a clinical thermometer at four hour intervals, the method employed in this work. For this reason and since only one infant was studied, the febrile increment for infants as given requires verification. It is conceivable that the metabolic gradient of fever in infants may be greater at higher levels of body temperature and in the presence of infection.

TABLE 9.—*Average Distribution of Calories in the Total Daily Energy Exchange (per Kilogram of Body Weight and in Terms of Percentage Rise Above the Basal Rate)*

Energy Component	Experimental Conditions	Number of Observations	Average Calories per Kg.	Percentage Rise Above Basal Rate: Average	Percentage Rise Above Basal Rate: Range
Basal quota	During sleep and on diets not exceeding the basal requirements	1*	57	..	.....
Activity quota	Awake and quiet for from 30 to 40 per cent of the twenty-four hours	8	8	14	6 to 18
Specific dynamic action	Basal diet	1	0	0	6 to 14
	Maintenance diets	5	7	11	
	High caloric diet	1	13	23	
Loss in feces	Basal diet	1	7	12	12 to 35
	Maintenance diets	6	9	16	
	High caloric diet	1	15	26	
Fever	101.7 F., average; 101.2 to 102.8 F. range	1	8	14	
Total catabolic requirements	Basal diet	1	73	26	24 to 67
	Maintenance diets				
	Without fever	5	82	41	
	With fever	1	90	55	
	High caloric diet	1	94	63	

* Only one infant was studied while on a basal dietary regimen (experiment 171). The basal rates for the other infants were predicted from published basal standards.[17]

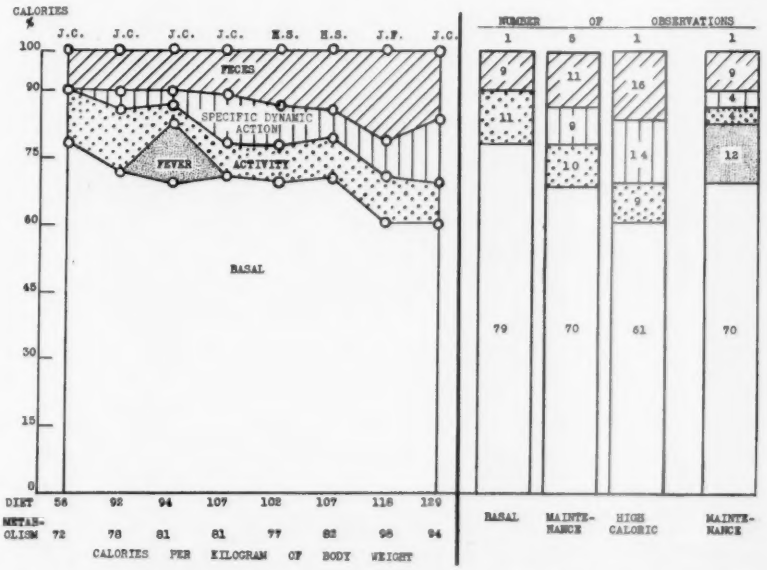

Fig. 1.—Percentage of calories contributed by the individual energy supplements to the maintenance metabolism. The chart on the left represents individual observations; that on the right, average figures for the three types of diet and in the presence of fever. The same plan of illustration is followed in the succeeding figures.

rise above basal levels, contributed by each energy supplement to the daily exchange are summarized in table 9. Figure 1 is arranged in ascending fashion according to the size of the diet to illustrate graphically the partition of all the energy factors, including the basal quota.

The daily energy requirements of the infants under conditions of limited activity varied with the nature of the daily diet. The calories necessary to cover the daily needs for maintenance ranged between 73 and 98 per kilogram for individual infants and were 73, 82 and 94 with the basal, maintenance and high caloric regimens, respectively. These average figures for the daily metabolism of the infants on the three types of diet represent metabolic accretions of 26, 41 and 63 per cent above their respective basal levels. The presence of a moderate grade of fever augmented the daily energy requirements of one infant an additional 14 per cent above the level previously established for his maintenance (table 9).

The partition of calories also varied with the size of the daily diet (fig. 1). The quotas contributed by specific dynamic action and by fecal loss rose from 0 to 14 per cent and from 9 to 16 per cent, respectively, at the expense of the basal quota, which correspondingly fell from the high level of 79 per cent to 61 per cent as the daily diet was shifted from a basal to a high caloric level. The activity quota, which formed around 10 per cent of the total exchange in these observations, on the other hand, was unrelated to diet and depended solely on the extent of muscular exertion.

If the results obtained in these observations are accepted as representative, the evidence would indicate that the daily energy requirements of healthy infants for maintenance exclusive of growth can be fulfilled as a rule by the administration of daily diets containing 40 per cent more calories than their basal requirement predicted from the body weight and stature, or in the neighborhood of 85 calories per kilogram of body weight in twenty-four hours.[25] Within a range in age of from 4½ to 9 months the maintenance needs were apparently not influenced by the age factor.

Twenty-Four Hour Caloric and Organic Balances in Normal Infants.—Analysis of the diet in conjunction with measurements of the respiratory metabolism and of the excreta provided the requisite data for drawing up daily balances of the calories and of the organic foodstuffs, protein, fat and carbohydrate. The energy balances in absolute amounts and on the basis of body weight are charted in figures 2 and 3. Figure 4 presents the balances for the organic substances.

25. It would seem desirable to add an extra increment of approximately 10 per cent to the calories of the diet as a margin of safety to cover any additional calories metabolized by infants in their natural environment as the result of heightened activity.

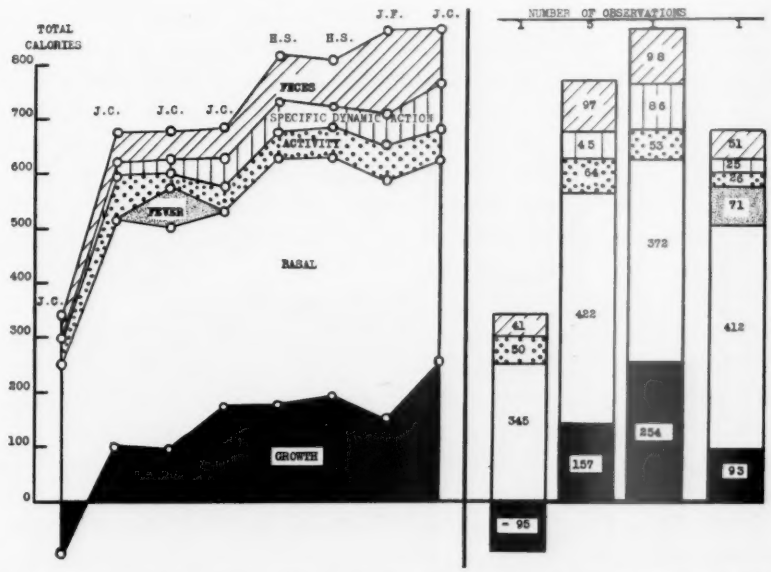

Fig. 2.—Caloric balances embodying the calories contributed by the individual energy supplements inclusive of the growth quota. The total height represents the caloric intake in each observation.

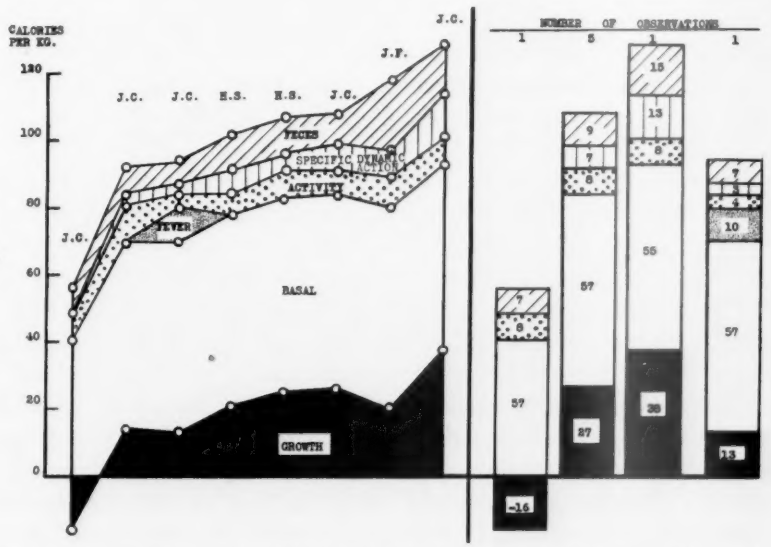

Fig. 3.—Same as figure 2 on the basis of body weight (calories per kilogram).

This method of illustration portrays graphically the relation of intake to output, with consequent body shifts of each of the constituents. Such synchronous and prolonged studies of energy and of organic balance have, to our knowledge, never before been attempted on normal infants.

In accordance with expectation, the calories available for body growth rose steadily with enhancement of the dietary calories. In infant J. C. a daily loss to the body of 95 calories with a basal diet of 56 calories per kilogram was converted to daily retentions of 101 and 171 calories and to a maximum retention of 254 calories as the caloric intake was progressively raised to maintenance levels of 92 and 107 and to the high caloric level of 129 calories per kilogram, respectively. In absolute amounts, the first-mentioned and last-mentioned diets contained 341 and 863 calories. Of the 522 calories making up the difference, only 349 were utilized for conversion of the negative to a positive balance, the 173 extra calories of the diet being expended in an augmented specific dynamic action (86), in an increased loss of calories in the feces (57) and in a higher basal rate (27).

The caloric retention within the body in the five observations with maintenance diets (108 calories per kilogram of body weight) averaged 157 per day (27 per kilogram) and varied between 101 and 193 for individual infants, the growth quota tending to parallel the size of the diet. The average growth quota with these diets, the caloric content of which closely approximated that of the formulas of cow's milk ordinarily employed in infant feeding, constituted 22 per cent of the total calories ingested.

For comparative purposes, caloric balances with the different dietary regimens are also given in terms of body weight (calories per kilogram per twenty-four hours) in figure 3. The interpretation of this figure differs in no way from that of the preceding one, and further comment is unnecessary.

The nature of organic shifts within the body is obviously as significant as the total caloric change in an appraisal of the adequacy of diets. A diet which permits the deposition of protein and the potential manufacture of protoplasm is incontrovertibly of greater value to the infant, in terms of optimal growth, than one which culminates in a more rapid accretion of body weight due to mere accumulation of fat in the body depots.

Figure 4 shows that with the exception of the observation in the presence of fever the daily retention of protein within the body was maintained at the relatively constant level of from 4 to 6 Gm. at all levels of protein intake between 4.1 and 5.6 Gm. per kilogram of body weight. Approximately 2 Gm. of protein was withdrawn daily from the body on the low intake of 2.5 Gm. per kilogram. No evidence is available from these observations regarding the magnitude of body stor-

age between and beyond these levels of protein intake, but if one accepts the customary figure of 14 per cent as representing the average protein content of muscle protoplasm the retentions as found with the adequate diets are commensurate with the daily building up of from 30 to 40 Gm. of protoplasmic tissue.

If practical application of these results to the art of infant feeding is permissible, one may assert with some assurance that the daily gain in body weight of from 15 to 30 Gm. usually achieved by the customary formulas employed in infant feeding of from 100 to 120 calories and

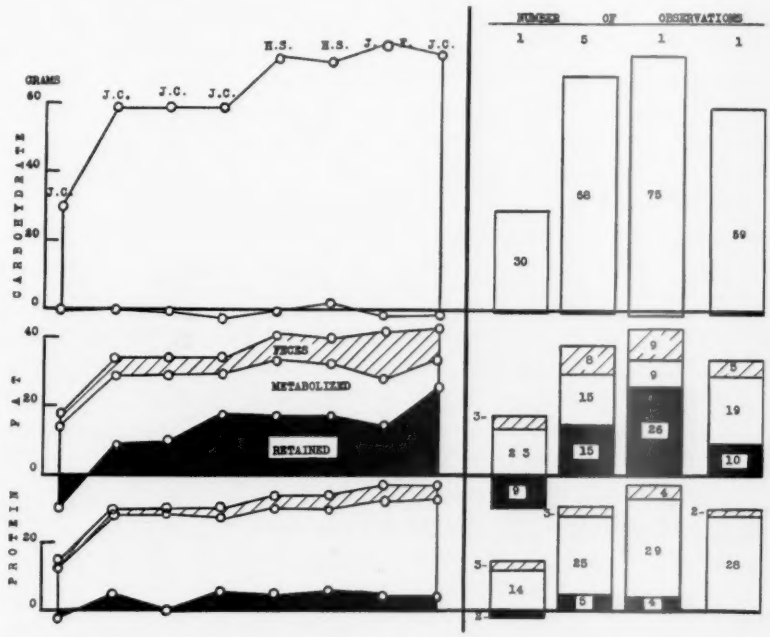

Fig. 4.—Organic balances. The lower charts represent the protein balance; the middle, the fat balance, and the upper, the carbohydrate balance.

from 4 to 5 Gm. of protein per kilogram of body weight is represented by the deposition of tissue of optimal composition. Analysis of the organic composition of body weight gained by J. C. while on the maintenance and high caloric diets lends support to the methods of feeding commonly used. As previously mentioned, the infant's daily retentions while he was on the two diets totaled 136 and 254 calories, of which protein contributed 5 and 4.3 Gm. (13 and 7 per cent) and fat, 13.2 and 25.9 Gm. (the remaining 87 and 93 per cent), respectively. The latter gain in weight with its inordinately high content of fat would not seem to be of particular advantage to normal well nourished infants and might even be deleterious if long continued.

Conclusive demonstration of the utilization of carbohydrate as a source of readily combustible material in the infantile organism is evident from the data. The infants invariably metabolized all the carbohydrate contained in the diet, which varied in these observations from as low as 30 to as high as 78 Gm. in twenty-four hours. Even at the latter high levels of intake no carbohydrate was available for storage in the body as glycogen. This evidence, procured under carefully controlled experimental conditions, confirms the well recognized but hitherto not definitely established dictum that infants as well as older persons burn carbohydrate by preference. In the presence of a plethora of carbohydrate in the diet the infantile organism maximally utilizes this material to meet its energy needs, and dietary fat is relegated in a large measure to the body reservoirs for storage. Only with a dearth of carbohydrate is fat drawn on to any extent to fulfil the energy requirements. At the levels of protein intake studied the metabolism of this foodstuff, as previously mentioned, remained practically constant. These relations between the several foodstuffs are more clearly visualized when the results are expressed in terms of percentages. The relative proportions contributed by protein, fat and carbohydrate to the metabolic mixtures were 15, 54 and 31 per cent with the basal regimen; 19, 27 and 54 per cent with the maintenance diets, and 23, 16 and 64 per cent with the high caloric regimen (table 6). If the caloric loss in the feces is included in the total output of energy, the respective percentages become 16, 56 and 28; 19, 35 and 46, and 18, 31 and 51, for the three types of diet. An inverse relationship between the combustion of fat and carbohydrate is seen to exist at all levels of diet.

The demonstration that normal infants receiving formulas of cow's milk ordinarily employed in infant feeding meet their energy needs by utilizing protein, fat and carbohydrate in average proportions of approximately 20, 35 and 45 per cent would suggest that on theoretical grounds at least formulas of this composition are optimally utilized by the infantile organism. Since, however, a plethora of either fat or carbohydrate in the diet leads to the deposition of fat within the body, these two foodstuffs would appear to be interchangeable in the diet in isocaloric amounts. The choice between the two types of foodstuffs in individual infants would seem to rest on such considerations as the tolerance of the alimentary tract, the factor of ketosis and analogous factors rather than on metabolic grounds alone.

COMMENT

The pediatrician should possess a knowledge of the nutritional principles at the basis of the current systems of infant feeding, especially since giving advice on the feeding of normal infants comprises a large part of his practice. This warning is particularly timely, as there is

a growing tendency among practitioners to prescribe fantastic diets for infants without regard to, and sometimes without knowledge of, their nutritional requirements.

The physiology of nutrition as it applies to infants may conveniently be considered under three headings: 1. The problem of the qualitative composition of diets. It is generally recognized that an adequate diet must contain a number of so-called essential elements, including the organic foodstuffs, protein, fat and carbohydrate, and water, at least ten inorganic substances and six vitamins. 2. The factor of palatability and digestibility to insure maximal utilization of the ingesta by the infantile organism. 3. The quantitative problem of the optimal concentrations of the different essential dietary factors.

Fortunately, nature has provided a food for infants in human and cow's milk which is digestible and which contains all the necessary factors except possibly iron, iodine and certain of the vitamins. Our chief interest, therefore, in this and succeeding papers of the series is with the quantitative composition of infants' diets.

From a quantitative standpoint, an ideal diet for infants may briefly be defined as one which contains all the essential components in sufficient amounts and in proper proportions to insure optimal growth and development. In practice an appraisal of the latter is commonly based on a number of clinical criteria and especially on the rate of gain in body weight. The latter is empirically classified as satisfactory if it is in the neighborhood of from 15 to 30 Gm. daily. That the daily accretions in body weight commonly achieved by the current methods of infant feeding are necessarily of optimal magnitude or that they represent the deposition within the body of materials of optimal composition has never been conclusively demonstrated.

Precise estimates of the qualitative constitution of the growth quota necessitate carefully controlled balance studies embracing the total intake, output and body shifts of each of the essential dietary factors. Such studies are time-consuming, technically difficult and heretofore not available for normal infants. This dearth of important data prompted the present balance studies of the organic foodstuffs and their energy equivalents and of water and a number of inorganic substances (sodium, potassium, phosphorus and chlorine). This paper presents the results of the studies of the first group of related foodstuffs; the results for the other substances will appear in succeeding papers,[6] and the practical application of these studies to the art of infant feeding will be summarized in the final paper of this series. Not until a sufficient number of similar studies under carefully controlled but varied conditions of diet and activity are available in the literature may the art of infant feeding be considered to be firmly established on a scientific basis.

SUMMARY AND CONCLUSIONS

Daily balance studies of the organic foodstuffs, protein, fat and carbohydrate, and their energy equivalents were made on three healthy infants of from 4 to 9 months of age while on basal, normal, high caloric and low fluid diets. The program consisted of eight observations embodying twenty-four hour measurements of the respiratory metabolism, concurrent analyses of the diet and excreta and accurate records of the behavior during the periods of observation. These studies formed part of a systematic investigation of the nutritional requirements of normal infants.

Under conditions of limited physical activity, the infants being awake and quiet for from 30 to 40 per cent of the twenty-four hours, the daily catabolic requirements were covered by 73, 82 and 94 calories per kilogram of body weight when the subjects were on the basal, normal and high caloric diets, respectively. These average figures for their maintenance metabolism while they were on the three types of diet represented metabolic accretions of 26, 41 and 63 per cent above their respective basal levels.

An average elevation of body (rectal) temperature to 101.7 F. due to dehydration (a low fluid diet) resulted in an extra expenditure of 10 calories per kilogram in twenty-four hours in one normal infant. The febrile increment in this infant was equivalent to a rise of 14 per cent above his established metabolic level in the absence of fever.

With the so-called normal diets which closely resembled those employed in infant feeding, the average apportionment of calories by the individual increments to the total daily catabolism of the three infants was as follows: basal quota, 57 calories per kilogram of body weight, or 70 per cent of the total exchange; specific dynamic action of food, 7 calories, or 9 per cent; activity quota, 8 calories, or 10 per cent, and loss in feces, 9 calories, or 11 per cent.

All the infants maintained positive caloric balances on the normal diets, and their growth quotas while they were on these diets were represented by the deposition within the organism of organic substances in proportions and quantities compatible with the building up of appreciable amounts of protoplasmic tissue. The evidence indicates that the customary diets employed in infant feeding, which contain approximately 110 calories and from 4 to 5 Gm. of protein per kilogram of body weight, are calorically and organically adequate to insure proper development, as determined by the amount and character of the materials made available to the infantile organism for the body growth of infants on these diets.

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BODY BUILD FACTOR IN THE BASAL METABOLISM OF BOYS

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In determining the nutritional status of a child many investigators independently have concluded that the body build factor must be considered. Franzen [1] in a comprehensive report gives all the possible skeletal measurements and their correlations with nutrition and health. Lucas and Pryor [2a] reported the use of the width-length index, which, as mentioned in a previous article,[3] I have found very practical. Lucas and Pryor [2b] stated: "The width-length index is an expression of the relationship of the width to the length of the body. It is obtained by measuring the diameter of the crest of the ilium and the standing height. The crest measurement is divided by the height to give the relative breadth of the body, or width-length index. This index represents width in per cent of standing height. Weight does not enter into the calculation. The size of the index increases with the relative breadth of the body."

Many boys who were formerly considered underweight were found to be average or even above average when their slender-built bodies were taken into consideration. Conversely, boys who were formerly considered overweight were found to be average or even below average when their broad-built bodies were taken into consideration. Palmer [4] ingeniously explained the necessity of taking into consideration the skeletal framework of a person. "The principal reason for variation in weight either side of the average weight for height is the differing widths and depths of children's bony framework. If the pantry shelf is only four inches wide, it will hold only one row of jars of jam. If

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1. Franzen, R.: Physical Measures of Growth and Nutrition, School Health Research, Monogr. 11, New York, American Child Health Association, 1931.

2. Lucas, W. P., and Pryor, H. B.: (*a*) Physical Measurements and Physiologic Processes in Young Children, J. A. M. A. **97**:1127 (Oct. 17) 1931; (*b*) The Body Build Factor in the Basal Metabolism of Children, Am. J. Dis. Child. **46**:941 (Nov.) 1933.

3. Molitch, M., and Eccles, A. K.: The Relation Between Nutrition, Mental Level and Adjustment in Delinquent Boys, J. Nerv. & Ment. Dis. **78**:123, 1933.

4. Palmer, T. G.: Is Weight a Measure of Your Child's Nutrition? Parents' Section, Junior Home J., January 1932.

the shelf is eight inches wide, it will hold two rows. The wider and deeper a child's skeletal shelf, the more room there is for muscle and fat."

Stockard [5] concluded: "The two groups into which almost all ordinary persons fall more or less exactly may, therefore, be termed the Linear and the Lateral Types. The linear type is the faster growing, high metabolizing, thin but not necessarily tall group, while the lateral type is slower in maturing and is stocky and rounder in form. Initial growth and rapid growth tend to produce linear structure." In the same article he stated that "an active thyroid gives fast growing, rapidly differentiating structures and linear rather than large lateral type individuals."

Lucas and Pryor [2b] found a definite relationship between body build and oxygen absorption in children. In their series of 573 girls and boys they found that "high basal metabolic rates as measured by the conventional standards are the rule for the linear type group, whose width-length indexes of body build are well below average." This means that the slenderly built children normally have higher basal rates than broad-built children of the same age-sex group. The same authors stated the belief that "the simple determination of the body build index is an adequate measure of this hereditary factor of build" and that "the type of bony framework possessed by a child is as unalterable a hereditary characteristic as the color of his eyes and the shape of his nose." It has been found necessary [3] to set up separate norms for each racial group. The Negro as a race has the linear type of body while the Italian has the lateral type of skeletal structure.

The fact that a child is apubertal, pubescent or pubertal is important when correlations of basal metabolic rate are made with other factors. Lucas and Pryor [2b] divided 184 boys into preadolescent and adolescent groups. They used boys from 3 to 9 years for the preadolescent and boys from 10 to 18 years for the adolescent group and found a negative correlation between basal metabolic rates and width-length indexes for the two groups. They concluded that the large width-length indexes are associated with the low basal metabolic rates and the small indexes with the high basal rates. In a previous article [6] it was shown that the arbitrary dividing of boys into age groups is not an accurate criterion of their state of adolescence. In 194 boys between the ages of 10 and 18, 34 were found to be apubertal, 60 were found to be pubescent and the rest pubertal (table 1). The differentiation in the three groups

5. Stockard, C. R.: Human Types and Growth Reactions, Am. J. Anat. **31**:26, 1923.

6. Molitch, M., and Cousins, R. F.: Variation of Basal Metabolic Rate per Unit Surface Area with Age, J. Nutrition **8**:247 (Aug. 10) 1934.

depended on the appearance of secondary sexual characteristics, such as pubic hair, down on the lips, axillary hair and change of voice.

Further, the basal metabolic rate during later childhood has been shown in numerous confirmatory investigations (Du Bois,[7] Bierring,[8] Göttche,[9] Topper and Mulier[10] and Molitch and Cousins[6]) to give indications of a definite increase, or an irregularity in decrease, related to age. Bruen[11] concluded: "The variation of the basal metabolic rate per unit surface area with age during the pubertal period may therefore be analyzed as the mathematical resultant of a fundamental decrease

TABLE 1.—*Variation in Number of Apubertal, Pubescent and Pubertal Boys in Each Age Group*

Age Group	Number of Boys	Apubertal	Pubescent	Pubertal
10–11	7	6	1	..
11–12	8	7	1	..
12–13	22	11	10	1
13–14	29	4	17	8
14–15	53	5	20	28
15–16	58	1	8	49
16–17	14	..	3	11
17–18	3	..	..	3

TABLE 2.—*Range of Indexes and the Basal Metabolic Rates of the Two Extremes in Each Age Group*

Age Group	Number of Boys	Range of Indexes	Basal Metabolic Rate of the Extremes (Calories per Kg. per Hour)
10	10	139 to 160	1.55 — 1.59
11	7	134 to 161	1.22 — 1.67
12	12	147 to 174	1.45 — 1.47
13	20	131 to 179	1.18 — 1.16
14	44	142 to 181	1.47 — 1.19
15	56	138 to 176	1.03 — 1.12
16	40	134 to 176	1.57 — 1.35

of the basal metabolic rate with age, and a superimposed cyclic acceleration. This cyclic acceleration of the basal metabolic rate is not a mere concomitant or effect of the adolescent growth cycle, but represents an independent pubertal metabolic acceleration."

7. Du Bois, E. F.: The Metabolism of Boys 12 and 13 Years Old Compared with the Metabolism at Other Ages, Arch. Int. Med. **17**:887 (June) 1916.

8. Bierring, E.: The Standard Metabolism of Boys (7 to 18 Years Inclusive), Copenhagen, Levin & Munksgaard, 1931, p. 118.

9. Göttche, O.: Gasstoffwechseluntersuchungen im Kindesalter. Die Pubertätsreaktion, Monatschr. f. Kinderh. **32**:22, 1926.

10. Topper, A., and Mulier, H.: Basal Metabolism of Normal Children: Puberty Reactions, Am. J. Dis. Child. **43**:327 (Feb.) 1932.

11. Bruen, C.: Variation of Basal Metabolic Rate per Unit Surface Area with Age: The Pubertal Acceleration, J. Nutrition **6**:383, 1933.

A total of 515 basal metabolic tests were made on 199 boys on whom width-length indexes had been obtained. The boys ranged in age between 10 and 18 years, the greater number being between 14 and 16. The boys to be tested were admitted to the hospital of the institution in the evening. No food was given after the evening meal and nothing to drink after midnight. Successive determinations were made every twenty-four hours until not more than a 4 per cent difference was

TABLE 3.—*Quartile Averages in Calories Per Square Meter for Each Age Group*

Age Group	Number of Boys	Quartile Averages (Calories per Sq.M.)			
		1	2	3	4
12	12	42.3	41.6	43.5	43.0
13	20	41.3	40.6	42.8	40.9
14	44	41.2	40.5	42.8	41.6
15	56	41.8	41.2	41.8	40.4
16	40	41.4	41.7	40.3	41.5

TABLE 4.—*Quartile Averages in Calories Per Kilogram Per Hour*

Age Group	Number of Boys	Quartile Averages (Calories per Kg. per Hour)			
		1	2	3	4
12	12	1.36	1.48	1.51	1.51
13	20	1.43	1.38	1.33	1.38
14	44	1.30	1.24	1.36	1.27
15	56	1.28	1.24	1.31	1.27
16	40	1.27	1.23	1.17	1.24

TABLE 5.—*Oxygen Consumption of Boys by Age Groups*

Age Group	Number of Boys	Total Calories per Hour	Average Calories per Hour	Total Calories per Kg. per Hour	Average Calories per Kg. per Hour
9	2	95.0	47.5	3.18	1.59
10	9	442.3	49.1	14.53	1.61
11	7	340.8	48.7	9.79	1.39
12	13	640.4	49.3	19.13	1.47
13	22	1,164.9	52.9	30.23	1.37
14	46	2,743.8	59.6	59.57	1.29
15	57	3,570.5	62.6	71.11	1.25
16	43	2,776.7	64.6	52.65	1.22

obtained. Averages of these check determinations were made. Many boys were excluded because of the inability to obtain a 4 per cent check on them or because of their nervousness. No boys with evident endocrine disturbances were used in the study. All of the tests were made with the Sanborn Motor-Grafic machine.

Correlations were made between the basal metabolic rates, as expressed in calories per square meter and in calories per kilogram per hour, and the width-length indexes. The findings of Lucas and Pryor [2b] were not confirmed. Each age group was studied and is reported

on separately in the tables. Table 2 gives the range of indexes and the basal metabolic rates of the two extremes in each age group. Table 3 gives the quartile averages in calories per square meter for each age group, while table 4 gives the quartile averages in calories per kilogram per hour. The first quartile in tables 3 and 4 represents the most linear type, while the fourth quartile in the same tables represents the most lateral type. It is seen, therefore, at a glance that in this series there is no definite relationship between body build and oxygen absorption. Boys of equal height but of varying indexes were compared, and the correlation with oxygen absorption was found to be negative.

In a personal communication of July 3, 1934, Dr. Helen B. Pryor recommended the elimination of the data for all boys whose bi-iliac diameters exceeded their lateral thoracic diameters by 3 cm. or more. She stated the belief that this asymmetry of the body is endocrine in origin and therefore not normal. It was possible at this time to examine again 34 of the boys of the original study, and only 3 of them fell into the category mentioned. One of these boys possessed a body build of feminine contour. Correlations between body build and mental level also were made, with negative results.

CONCLUSIONS

Correlations between body build and oxygen absorption were found to be absent in 199 boys.

In this series higher basal metabolic rates were not characteristic of the linear type of body build.

FAMILIAL STUDIES ON LOBAR PNEUMONIA

EPIDEMIOLOGIC STUDIES ON FAMILIES OF CHILDREN WITH PNEUMOCOCCIC LOBAR PNEUMONIA

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The family group in pediatric practice has a cohesiveness which invites epidemiologic study. Lobar pneumonia would seem to be susceptible to profitable investigation by this method. Indeed, Shultz [1] has already reported her findings in the families of twenty-one children with this disease. Her results were much the same as those of Stillman,[2] Jacobson,[3] Rosenau, Felton and Atwater,[4] Smillie and Caldwell,[5] Smillie [6] and Smillie and Leeder,[7] who used this method but were not particularly concerned with observations on children.

The material for the present communication is similar to that of Shultz. We had fourteen families, about half as many as Shultz, but since we studied each member of every household the total number of subjects in the two series is about the same. In taking the histories we paid close attention to all symptoms, even to those of a minor nature, because in many children so-called primary lobar pneumonia is preceded by a common cold and, furthermore, because we were interested to learn the general pattern of infections of the upper respiratory tract

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1. Shultz, S. M.: Study of Certain Epidemiological Factors in Pneumonia of Children, Am. J. Hyg. **15**:80 (Jan.) 1932.

2. Stillman, E. G.: A Contribution to Epidemiology of Lobar Pneumonia, J. Exper. Med. **24**:651 (Dec.) 1916; Further Studies in Epidemiology of Lobar Pneumonia, ibid. **26**:513 (Oct.) 1917.

3. Jacobson, M. A.: Observations on Epidemiology of Lobar Pneumonia, J. Prev. Med. **1**:259 (Jan.) 1927.

4. Rosenau, M. J.; Felton, L. D., and Atwater, R. M.: Epidemiologic Study of Pneumonia and Its Mode of Spread, Am. J. Hyg. **6**:463 (May) 1926.

5. Smillie, W. G., and Caldwell, E. L.: Study of Pneumonia in Rural Area in Southern Alabama, J. Exper. Med. **50**:233 (Aug.) 1929.

6. Smillie, W. G.: Epidemiology of Lobar Pneumonia: Study of Prevalence of Specific Strains of Pneumococci in Nasopharynx of Immediate Family Contacts, J. A. M. A. **101**:1281 (Oct. 21) 1933.

7. Smillie, W. G., and Leeder, F. S.: Epidemiology of Lobar Pneumonia, Am. J. Pub. Health **24**:129 (Feb.) 1934.

in the families concerned. We were also interested in correlating the age of the various subjects with the presence of pneumococci in cultures of material from their throats.

MATERIAL AND METHODS

The material consists of the cases of all the patients with lobar pneumonia admitted to the pediatric service of New Haven Hospital from January to July 1932. The period in question was unusually poor with regard to pneumonia, for the total number of admissions for this disease in the pediatric and medical services of the hospital was about half the mean figure for the previous ten years.

A visit was made to the home of each patient within two or three days after the diagnosis of lobar pneumonia had been established. The history of each member of the household was obtained in full detail, the family having been aided by a calendar placed before them together with a list of all possible symptoms of infection of the upper respiratory tract. Particular attention was paid to symptoms noted during the four weeks preceding the patient's illness. Return visits to the home were not made regularly, but the family was followed up by questioning the parents during the patient's stay in the hospital, which generally covered a period of more than two or three weeks.

Material for culture was taken from each member of the family by swabbing the pharynx with a sterile cotton-armed swab which was immediately introduced into a tube containing several cubic centimeters of infusion broth. At the hospital the swab was streaked on a blood agar plate and a white mouse was inoculated intraperitoneally with 1 cc. of the broth.

On the blood agar plate, twenty-four hours later, we noted the variety and relative number of different organisms present. The mouse was allowed to die or was killed at the end of fourteen days,[8] and an autopsy was done in the usual manner by the customary bacteriologic technic. The peritoneal washings were used to determine the type or types of pneumococci present.

During the first month of our study we used the macroscopic method of typing pneumococci against antiserums of types I, II and III. For the remaining period we used the Sabin slide agglutination[9] method against the thirty-two (Cooper) type-specific serums[10] furnished us through the courtesy of Dr. Georgia Cooper of the Bureau of Laboratories of the Board of Health of the City of New York.[11]

OBSERVATIONS

Bacteriologic.—As will be noted in table 1, the bacteriologic findings were in general similar to those reported by others. The most interesting feature in the table is the high incidence of pneumococcus carriers.

8. The mice that survived fourteen days showed no pneumococci in the peritoneal cavity.

9. Sabin, A. B.: Microscopic Agglutination Test in Pneumonia; Its Application to Rapid Typing and Control of Serum Therapy, J. Infect. Dis. **46**:469 (June) 1930.

10. Cooper, G.; Rosenstein, C.; Walter, A., and Peizer, L.: Further Separation of Types Among Pneumococci Hitherto Included in Group IV and Development of Therapeutic Antisera for These Types, J. Exper. Med. **55**:531 (April) 1932.

11. During the early period the unclassifiable pneumococci have been designated as group IV and during the latter, as "unclassifiable."

The figure is 74 per cent and is to be compared with the high point of the seasonal variation in the general incidence of pneumococcus carriers, which Smillie [6] found to be 63 per cent. Another interesting feature is the strong relationship between age and the carrier which corroborates the observations of Gundel and Linden [12] that children are especially prone to be carriers of pneumococci.

Pneumococcus type III, which was recovered eleven times, was the most common of the fixed types found in the carrier state, and type

TABLE 1.—*Incidence of Carriers of Pneumococcus and Its Relation to Age in Members of the Family Exposed by Contact*

Age, Years	Pneumococci in Throat			Type of Pneumococcus											
	Present	Absent	Positive, %	I	II	III	IV	VIII	XII	XIV	XXII	XXVIII	XXX	Unclassified	Group IV
Under 1	6	0	100	..	..	..	1	1	..	..	..	..	..	2	2
1 to 5	13	0	100	..	..	1	..	..	1	1	..	..	..	6	4
6 to 11	18	4	81	..	..	4	..	1	..	..	1	1	..	7	5*
12 to 20	4	6	40	..	..	2	..	..	..	..	1	..	..	..	1
21 to 30	3	2	60	..	..	..	..	..	..	..	..	..	1	2	..
31 to 40	10	7	58	1	..	2	..	2	..	..	..	..	..	5	2*
41 to 60	5	2	71	1	..	2	..	..	..	..	..	..	..	2	..
Total	59	21	74	2	..	11	1	4	1	1	2	1	1	24	14*

* The discrepancy between the total number of various types of pneumococci recovered and the total number of carriers is explained by the finding of more than one type of pneumococcus in a given carrier.

TABLE 2.—*Incidence of Contact Carriers of Homologous Types in Families of Patients with Pneumococcic Pneumonia of Fixed Type* *

Type	Number of Cases	Number of Persons Exposed by Contact	Persons Exposed Having Positive Cultures	Percentage
I	3	21	2	9
III	2	11	3	27
VI A	3	23	0	0
VIII	1	3	3	100
XI	1	5	0	0
XIV	1	4	0	0
Total	11	67	8	12

* Three cases of unclassified pneumococcus pneumonia with twenty-seven contacts have been omitted for obvious reasons.

VIII, isolated four times, was the next most common. Pneumococcus type II did not appear during this study either among the patients or among the persons in contact with them, and in general cases of this type have been uncommon in New Haven.

Table 2 indicates the incidence of contact carriers of homologous types in the families of our patients with a specific type of pneumococcic pneumonia, and in table 3 our results are compared with those described

12. Gundel, M., and Linden, H.: Ueber die Verbreitungsweise der Menschlichen Pneumokokkeninfectionen, Ztschr. f. Hyg. u. Infectionskr. **112**:1 (Jan.) 1931.

by other investigators. It appears from table 3 that pneumococcus types II, III, V and VIII show a higher correlation between patients and persons exposed to them by contact than do the other types. It should be added that while type I shows an average correlation of but 7.7 per cent its distribution in the general population is less than 1 per cent so

TABLE 3.—*Data on Incidence of Pneumococci in Members of the Family as Reported in the Literature*

Type	Author	Number of Cases	Total Number Exposed	Persons Exposed Having Positive Cultures	
				Number	Percentage
I	Stillman [2] 1916	24	44	2	4.5
	Stillman [3] 1917	28	107	15	15.0
	Jacobson [3] 1926	16	36	6	17.0
	Rosenau, Felton and Atwater [4] 1926	..	216	8	3.7
	Smillie and Caldwell [5] 1929	..	17	2	11.7
	Shultz [1] 1931	6	21	5	23.8
	Bunim and Trask 1932	3	21	2	9.5
	Smillie [6] 1933	48	186	10	5.4
	Smillie and Leeder [7] 1934	17	62	15	24.2
	Total		710	65	9.1
II	Stillman	17	40	3	7.5
	Stillman	24	77	5	6.5
	Jacobson	7	29	14	48.0
	Smillie and Caldwell	..	7	3	42.8
	Shultz	4	16	0	0.0
	Smillie	34	126	14	11.1
	Smillie and Leeder	10	37	6	16.2
	Total		332	45	13.5
III	Rosenau, Felton and Atwater	..	54	6	11.2
	Shultz	2	7	2	28.5
	Bunim and Trask	2	11	3	27.2
	Smillie	16	61	13	21.0
	Total		133	24	18.0
IV	Shultz	1	5	0	0.0
V	Shultz	2	7	1	14.2
	Smillie	8	32	5	15.6
	Total	10	39	6	15.4
VI	Shultz	3	14	1	7.1
	Bunim and Trask	3	23	0	0.0
	Smillie	3	6	1	16.7
	Total	9	43	2	4.6
VII	Shultz	2	11	2	18.1
	Smillie	8	31	1	3.2
	Total	10	42	3	7.0
VIII	Bunim and Trask	1	3	3	100.0
	Smillie	12	31	7	20.1
	Total	13	34	10	29.4
IX	Shultz	1	5	0	0.0
	Smillie	2	15	4	31.0
	Total	3	20	4	20.0
XI	Bunim and Trask	1	5	0	0.0
XIV	Bunim and Trask	1	4	0	0.0
	Smillie	1	2	1	50.0
	Total	2	6	1	16.7
XVIII	Smillie	7	23	4	17.4

that, as Stillman has already pointed out, its epidemiologic significance is of considerable importance.

Clinical.—In table 4 we have correlated our clinical with our bacteriologic observations and in the figure this correlation is graphically illustrated.

The following observations will be noted in table 4: 1. Of the entire group of forty-one persons below 11 years exposed by contact with the patient only four, or 10 per cent, had no pneumococci in cultures from the throat, whereas of thirty-nine of those above 11 years, seventeen, or 43 per cent, had no pneumococci. 2. Forty-six per cent of those exposed below 11 years had symptoms of an infection of the upper respiratory tract in contrast to only 20 per cent of those above 11

TABLE 4.—*Correlation of Clinical and Bacteriologic Observations*

	Below 11 Years (41 Exposed)		Above 11 Years (39 Exposed)	
	No Symptoms at Time of Culture	Symptoms at Time of Culture	No Symptoms at Time of Culture	Symptoms at Time of Culture
I	..	..	1	1
II	..	..	..	..
III	1	4	5	1
IV	..	1	..	..
VIII	2	..	2	..
XII	..	1	..	..
XIV	1	..	..	..
XXII	1	..	1	..
XXVIII	..	1	..	..
XXX	..	..	1	..
Unclassified	8	7	5	4
Group IV	6	5	3	..
No pneumococci	3	1	12	5
Total	21*	20	28*	11

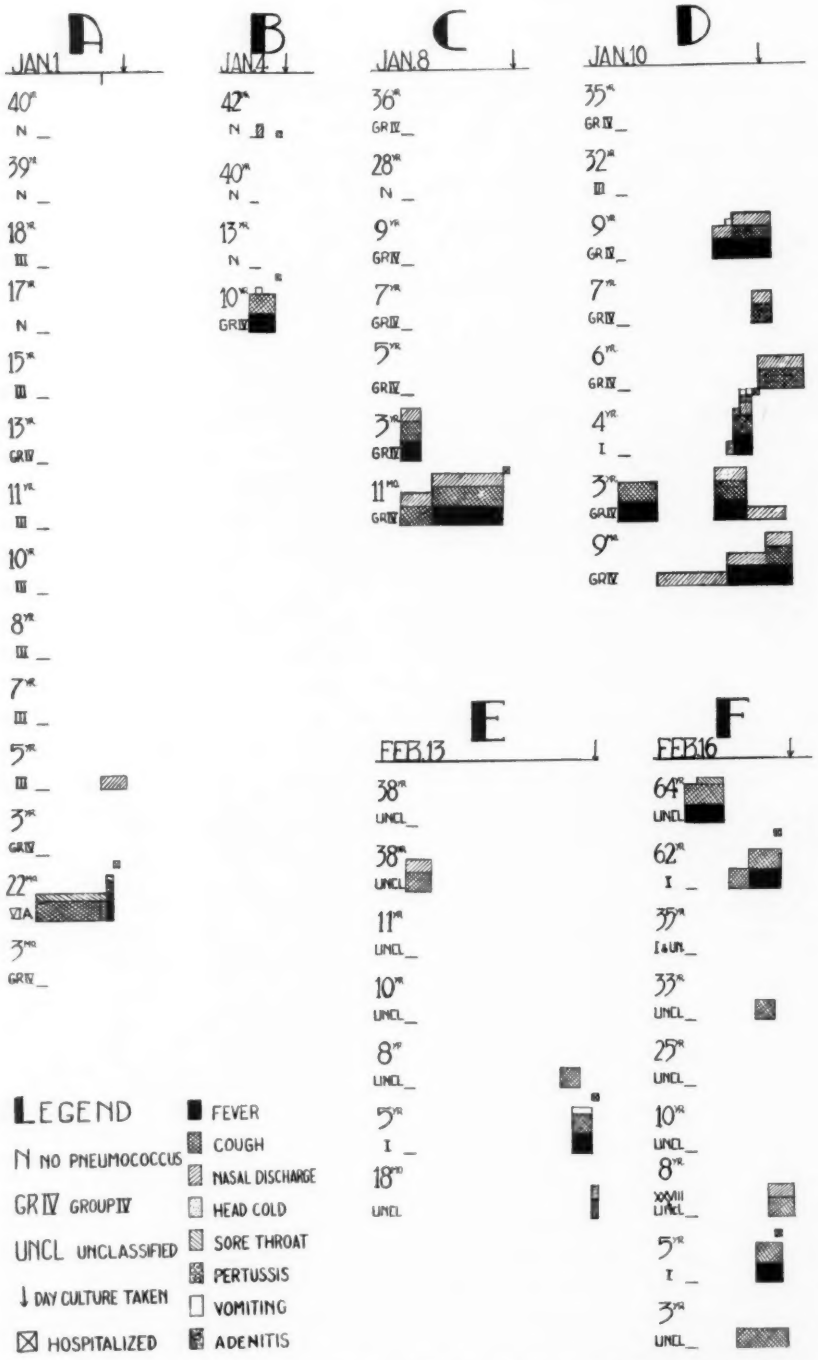
* The discrepancy between the total number of various types of pneumococci recovered and the total number of carriers is explained by the finding of more than one type pneumococcus in a given carrier.

years. 3. Of those exposed above 11 years, those who had no respiratory infections harbored pneumococci in their throats just as frequently as those who had symptoms, but of those exposed below 11 years, 13 per cent of the symptom-free children carried no pneumococci in contrast to only 5 per cent of those who had symptoms. 4. Four of the five persons exposed below 11 years who were carriers of the type III pneumococcus had symptoms of an infection of the upper respiratory tract, whereas only one of the six above 11 years who were carriers of type III had such symptoms.

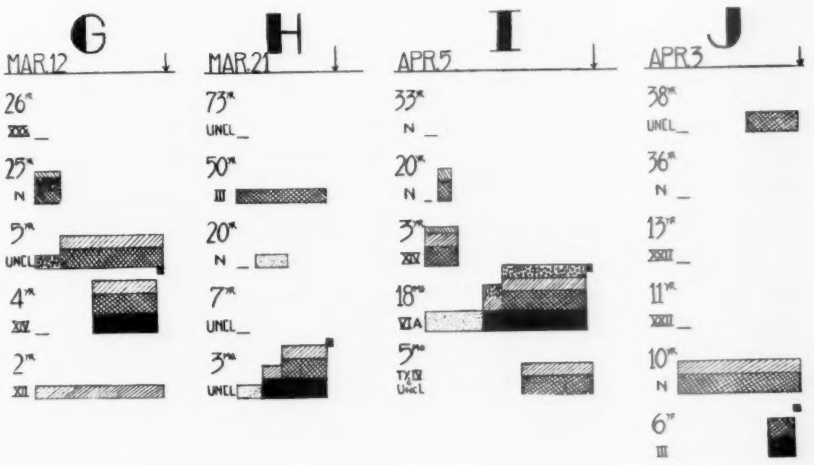
The chart represents graphically the fourteen families studied and their ninety-four members. The families are represented as *A, B, C,* etc. A space has been devoted to each member, with the age and type of pneumococcus recovered from culture inserted to the left. The symbol of the small square and crossed diagonals, denoting hospitalization, appear above and to the right of the patient with lobar pneumonia. One side of the square also measures one day in the figure.

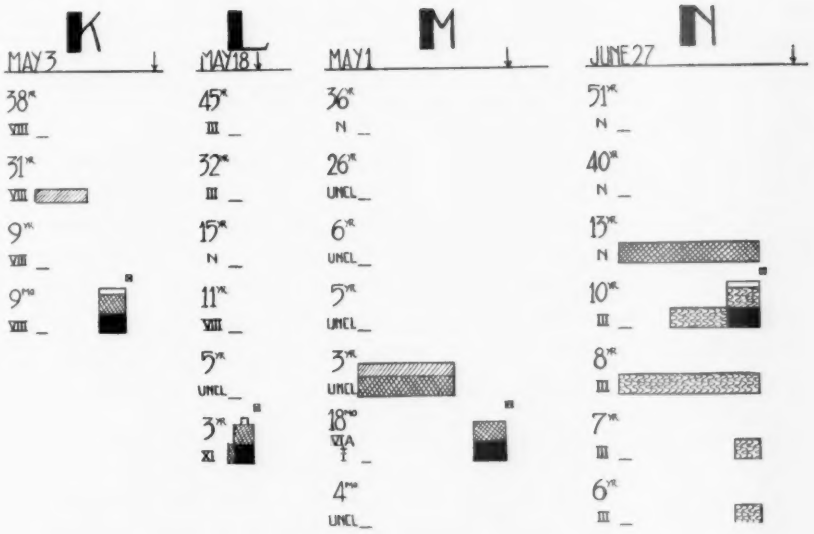
It is interesting to note the following points emphasized in this chart: 1. Twelve of the fourteen patients with lobar pneumonia were either the youngest or next to the youngest member of the family. 2. In thirteen of the fourteen families one or more members besides the patient gave a history of an infection of the upper respiratory tract. In six families there was an epidemic of disease of the respiratory tract. 3. There was one family (*F*) in which there was more than one case of pneumonia, and in four other families (*D, E, I* and *N*) the symptomatology in some of the members exposed by contact was that of a moderately severe infection of the respiratory tract. In the *F* family the events were as follows: On February 16 the great uncle aged 64 had fever and a cough. On February 18 sore throat ensued and he took to bed. He became free from symptoms on February 22. On February 23 the grandmother aged 62 began to cough. February 26 marked the onset of pneumonia, and on March 1 she entered a hospital, where she died of lobar pneumonia on March 3. Pneumococcus type I was recovered from her sputum. On February 24 the 3 year old sister had a cough, which cleared up on March 3. She had no severe symptoms. On February 27 the patient, aged 5, had fever, irritability and cough. On February 28 his temperature was 104 F. and he suffered pain referred to the left side of his chest. The following day he had a convulsion, and on March 1 he was admitted to the New Haven Hospital, where on March 3 he had a typical crisis with recovery from lobar pneumonia. Pneumococcus type I was isolated from his throat. February 27 marked the onset of cough and pain in the chest in the father, aged 33. His symptoms were mild, and they disappeared by March 1. On February 29 the 8 year old brother had a cold and nasal discharge. He was only mildly sick and became free from symptoms by March 4. The family was visited, and all members except the grandmother were studied bacteriologically on March 3. The results are shown in the chart. On a return visit on March 10, cultures were taken again and the same results were obtained as before except that the uncle, aged 35, who lived in the same home and was free from symptoms, was found this time to be a carrier of the pneumococcus type I.

Among the four families (*D, E, I* and *N*) having examples of moderately severe illness, the members of family *D* suffered most. Fortunately our visit was made while the epidemic in the family was still in progress. Although the sister aged 9 and the sister aged 3 were sick in bed, neither had signs or symptoms of pneumonia and both recovered without incident. However, from none of the family except the patient was the pneumococcus type I isolated.



A graph of the observations made on the members of the families of fourteen patients with pneumococcic pneumonia. This section includes observations on families *A* to *F*.





This section includes observations on families *G* to *N*.

COMMENT

In pneumococcic pneumonia due to the highly parasitic pneumococcus of type I or type II Stillman [2] demonstrated an increased carrier rate of the homologous pneumococcus among members of infected families. This observation has been corroborated amply by subsequent investigators and recently has been amplified by Smillie and Leeder.[7] The latter authors found that three quarters of the members of the families exposed by contact and carrying pneumococci homologous with the type found in the patients had colds at the time the cultures were taken. By and large our results are similar to those already mentioned, but we found that the increase in the incidence of carriers of pneumococci was related to heterologous as well as to homologous types. Moreover, the increase was related to the youth of the subject and to the presence of symptoms of infection of the upper respiratory tract in the younger subjects.

In comparing our results with those of others it is to be recalled that our patients were recruited from a pediatric service and that all members of the families were studied. Unfortunately, our series was small and contained no adequate controls. To be sure, the general distribution of pneumococci is pretty well known; nevertheless there are no extended data on the relation of age or infection of the upper respiratory tract to the number of carriers except that Gundel and Linden [12] have reported that the carrier state is most common in school children of the age group of lowest incidence of pneumonia and Dochez [13] and Webster and Clow [14] have commented on the increased numbers of pneumococci in the upper respiratory tract following the common cold.

In view of the recent publications of Dochez [13] and Shope [15] the interesting features of the present study are the results embodied in the chart, which shows the general background of symptomatology of the respiratory tract in families in which pneumonia has occurred. The data are too limited to do more than draw attention to the frequency of the positive findings. It is obvious that when pneumonia occurred in a child it was common to find others in the family with some form of infection of the respiratory tract.

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13. Dochez, A. R.: A Limited Consideration of Certain Aspects of Acute Infection of the Respiratory Tract, Medicine **12**:245 (Sept.) 1933.

14. Webster, L. T., and Clow, A. D.: Association of Pneumococci, Hemophilus Influenzae and Streptococcus Hemolyticus with Coryza and Sinusitis in Man, J. Exper. Med. **55**:445 (March) 1932.

15. Shope, R. E.: Swine Influenza: Filtration Experiments and Etiology, J. Exper. Med. **54**:373 (Sept.) 1931.

SUMMARY

A combined clinical and bacteriologic epidemiologic study has been made in the families of fourteen children with pneumococcic pneumonia. The results indicate (1) that youth and the presence of symptoms of infection of the upper respiratory tract in the younger subjects favor the carrier state of homologous and heterologous pneumococci, and that (2) infection of the upper respiratory tract is common in families in which pneumococcic pneumonia occurs.

OCCURRENCE OF TUBERCLE BACILLI IN THE BLOOD OF THE UMBILICAL CORD AND IN THE NEW-BORN INFANTS OF TUBERCULOUS MOTHERS

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The frequency with which tubercle bacilli are carried in the umbilical blood stream from the placenta to the fetus is not well known. If one judges by the incidence of demonstrable tuberculous lesions in the fetus and in the new-born infant, the transmission of the bacilli by way of the umbilical vein is extremely rare. Cases of undoubted congenital tuberculosis in a stillborn infant [1] and in several new-born infants dying soon after birth with generalized tuberculosis [2] are cited in the literature. In these cases the lesions were usually most marked in the liver and its regional lymph nodes.

There is evidence, however, that the tubercle bacilli might be transmitted by way of the umbilical vein more frequently than is indicated by the finding of tuberculous lesions in the fetus and in the new-born infant. Cases have been reported in which tubercle bacilli were present in the fetus, although there were no demonstrable lesions. In these instances, tuberculosis developed in guinea-pigs inoculated with specimens of apparently normal liver, spleen and lung.[3] There are similar findings in new-born infants dying soon after birth.[4] The presence of tubercle bacilli in tissue free from visible tuberculous lesions suggests, among other possibilities, a very recent infection. This might

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1. Whitman, R. C., and Greene, L. W.: A Case of Disseminated Miliary Tuberculosis in a Still-Born Fetus, Arch. Int. Med. **29**:261 (Feb.) 1922.

2. Lehmann, F.: Berl. klin. Wchnschr. **31**:646, 1894. Rollett, H.: Wien. klin. Wchnschr. **26**:1274, 1913. Ustinow, A.: Arch. f. Kinderh. **25**:66, 1898. Auche and Chambrelant: Arch. de méd. expér. et d'anat. path. **11**:534, 1899. McCord, J.: Am. J. Obst. & Gynec. **19**:826, 1930. Stoeckel: München. med. Wchnschr. **51**:177, 1904. Wollstein, M.: Arch. Pediat. **22**:321, 1905. Siegel, M.: Am. Rev. Tuberc. **29**:297, 1934.

3. (*a*) Wassermann, A.: Ztschr. f. Hyg. u. Infektionskr. **17**:343, 1894. (*b*) Schmorl and Birch-Hirschfeld: Beitr. z. path. Anat. u. z. allg. Path. **9**:428, 1890. (*c*) Landouzy and Martin: Rev. de méd., Paris **11**:415, 1891. (*d*) Warthin, A. S., and Cowie, D. M.: J. Infect. Dis. **1**:140, 1904. (*e*) Heitz, J.: Rev. de la tuberc. **9**:271, 1902.

4. Schmorl and Köckel: Beitr. z. path. Anat. u. z. allg. Path. **16**:316, 1894. Thiercelin, E., and Londe, P.: Méd. mod. **4**:398, 1893.

occur during delivery, when the trauma of labor disrupts the tuberculous areas in the villi and in the placental sinuses and frees the tubercle bacilli for dissemination in both the child and the mother.

Furthermore, tuberculous areas in the placenta have been found frequently by some investigators. Of twenty-six placentas examined by Sitzenfrey,[5] tuberculous lesions were found in six (23 per cent). Schmorl and Geipel[6] were even more successful; of twenty placentas, they found tuberculous lesions in nine (45 per cent). In some cases the lesions were large and easily visible. In others the lesions were so small that they were discovered only on microscopic examination. For example, in the series reported by Schmorl and Geipel, of the nine tuberculous placentas there were macroscopic lesions in three, while six were found to contain tuberculous lesions on microscopic examination. In one case, about two thousand microscopic sections had to be examined before a tuberculous area was seen. In Sitzenfrey's series, the search in one placenta took six months before a tuberculous area was found. Such instances show how minutely the placenta must be examined, and that a negative finding in the placenta is only relatively negative.

Patients in whom tuberculosis of the placenta was found usually had advanced pulmonary tuberculosis, with or without clinical evidence of generalized miliary dissemination. However, tuberculosis of the placenta may be found when there is little pulmonary involvement in the mother, such as a small apical lesion.[6] This possibility can be explained by the fact that tuberculous bacillemia may occur early in the course of tuberculosis.

The duration of pregnancy is important, for it takes time for the placenta to be formed and for the bacilli in the maternal blood stream to infect the placenta and produce lesions. It is therefore rare to find tuberculosis of the placenta in a patient in the early stages of pregnancy. In those in whom tuberculosis of the placenta was found, the period of gestation usually had been more than four months. Similarly, it is rare to find tubercle bacilli or tuberculous lesions in the fetus before the fifth month of pregnancy. Pankow[7] found no evidence of the presence of tuberculosis in the fetuses of seventeen tuberculous mothers who had been pregnant from three to four months. And in no instance did tuberculosis develop in guinea-pigs inoculated with specimens of liver and spleen from each fetus.

Tuberculous lesions in the placenta develop in the intervillous blood spaces if the portal of entry is the blood stream, as it usually is. The original site of the lesion in the placental sinus is not known definitely.

5. Sitzenfrey, A.: Die Lehre von der kongenitalen Tuberkulose mit besonderer Berücksichtigung der Placentartuberkulose, Berlin, S. Karger, 1909.

6. Schmorl and Geipel: München. med. Wchnschr. **51**:1676, 1904.

7. Pankow: Monatschr. f. Geburtsh. u. Gynäk. **32**:579, 1910.

Some investigators [8] have stated the belief that it begins on the damaged syncytium of a villus. Whatever the site of origin, it is noteworthy that the tuberculous lesion begins and develops in the intervillous blood spaces as a thrombus containing tubercle bacilli. The lesion might be so minute as to be visible with the microscope only, or so massive as to be easily seen with the naked eye. The involvement of the villi varies from a minute tuberculous area on the surface of the villus, the syncytial lining of which might still be intact, to varying degrees of invasion into one or more villi, occasionally with extensive caseation. Many of the capillaries of the villi are filled with thrombi, some of which contain tubercle bacilli. The bacilli are also seen occasionally among the red blood cells in the patent capillaries of the villi,[6] from which they enter directly into the umbilical vein. In the intervillous blood spaces, the bacilli have been found free or enmeshed in masses of fibrin and hyalin, in agglutinated red blood cells and in caseous masses. From these sources, the bacilli can enter the maternal circulation, and perhaps the fetal circulation, when the villi are traumatized during labor.

METHOD OF STUDY

In the present study, we were interested especially in the frequency with which tubercle bacilli could be detected in the umbilical blood. There were fifteen infants, all born of tuberculous mothers. In each case, two specimens of umbilical blood were collected immediately after the child had been born and the umbilical cord cut. Each specimen contained from 5 to 10 cc. of blood which was thoroughly shaken with 2 cc. of 10 per cent sodium citrate to prevent clotting and cultured for tubercle bacilli by the Loewenstein method.[9] This method involved the removal of hemoglobin with 3 per cent acetic acid or sterile distilled water, the use of from 0.5 to 1 cc. of 15 per cent (by volume) sulphuric acid to destroy contaminants and the inoculation of the whole residue on Loewenstein's congo red medium in from five to six culture tubes. The tubes were sealed with sealing wax, incubated at 38 C. and examined at weekly intervals for macroscopic growths of tubercle bacilli. Negative cultures were kept for two months and discarded after microscopic examination of a smear from the surface of the medium showed no acid-fast bacilli. Cultures suspected of having tubercle bacilli were subcultured and tested for virulence by inoculation of guinea-pigs.

The new-born infants were isolated immediately after birth in a nursery where they were observed for evidence of tuberculosis by repeated intracutaneous tests with from 1 to 10 mg. of tuberculin and by physical and roentgen examination. Necropsies were performed on those who died, and blood from the heart and specimens of liver, spleen and lungs were taken for culture of tubercle bacilli by the Loewenstein method.

The mothers were observed clinically, with particular attention given to the duration of pregnancy, to the nature and extent of tuberculosis and to the postpartum course. In five instances, specimens of blood were taken from the patient before and immediately after labor to see if tuberculous bacillemia had occurred as a result of labor.

8. Sitzenfrey.[5] Warthin, A. S., and Cowie, D. M.[3d]
9. Loewenstein, E.: Acta path. et microbiol. Scandinav. **10**:60, 1933.

RESULTS

In the 15 cases in which umbilical blood was taken, there was one positive culture. In this instance the primary culture had two minute, grayish-white colonies close together at the side of the medium. On subculture, a luxuriant growth of grayish-white, coarse colonies, resembling colonies of tubercle bacilli, appeared over the surface of the medium. An emulsion of the subculture was injected into the subcutaneous tissue of the left thigh of three guinea-pigs. Two of the animals died with nontuberculous pneumonia three days after the inoculation. The third died in two months with enlarged, caseous regional inguinal and retroperitoneal lymph glands, caseous hilar nodes and an enlarged spleen filled with miliary tubercles. Cultures of the regional inguinal glands, of the hilar glands and of the spleen were studded with colonies of tubercle bacilli.

The placenta in this case had a necrotic tuberculous area, 2 cm. in diameter. Microscopic examination of the involved area showed caseous masses in the placental sinuses, extensive tuberculous involvement of numerous villi and many acid-fast bacilli in the tuberculous areas.

The infant was born prematurely at 7 months, weighing 1,100 Gm. and measuring 35 cm. in length. He was inactive, weak and cyanotic. His respirations were shallow, infrequent and accompanied by a very weak cry. Attempts at restoration with respiratory stimulants and artificial heat were futile, and the child died three hours after birth. Clinically, there was no evidence of disease, and the cause of death was attributed to prematurity.

The postmortem examination was performed six hours after death. The macroscopic findings were negative except for numerous atelectatic areas in the lungs. There was no evidence of tuberculosis in the liver and its regional lymphatic glands, in the spleen or in the lungs. Microscopic examination of numerous areas in the liver, spleen, lungs and kidneys showed no evidence of tuberculous lesions or of acid-fast bacilli. Sections of the lungs showed marked dilatation of the blood vessels, with infiltration of red blood cells and of serum in the interstitial tissue and alveolar sacs. The final diagnosis was prematurity and atelectasis of the lungs.

A culture of the blood for tubercle bacilli was made from 2 cc. of blood from the heart which was aspirated, under sterile conditions, from the right auricle by means of a syringe and wide bore needle. In three weeks, innumerable, minute gray colonies were visible over the surface of the medium in all the culture tubes. The colonies were typical growths of tubercle bacilli. They grew readily on subculture, and on subcutaneous injection into guinea-pigs they produced caseous involvement of the regional lymphatic glands and generalized miliary tuberculosis.

The mother was 26 years old and of Italian descent. She was a primipara whose last menstrual period had occurred in September 1932. On admission to Sea View Hospital in March 1933, her uterus was enlarged to the level of the umbilicus. She had bilateral destructive pulmonary tuberculosis with laryngeal and gastro-intestinal involvement, sputum which contained tubercle bacilli and a daily intermittent rise of temperature to 103 or 104 F. She was moderately emaciated, and her general condition was poor. On April 25, she had a precipitate labor about twenty minutes after the onset of severe labor pains. Her general condition rapidly became worse with the appearance of cyanosis, dyspnea and tachycardia. On the following day, about eighteen hours after delivery, the patient died.

To recapitulate, tubercle bacilli were cultured from the umbilical blood and the blood taken post mortem from the heart of an infant born prematurely at

7 months who died three hours after birth with no demonstrable tuberculous lesions. There was a large tuberculous lesion in the placenta. The mother died of tuberculosis eighteen hours after the delivery.

There were fourteen new-born infants, cultures of whose umbilical blood were negative for tubercle bacilli. Of these, four died within the first month, and ten are still alive. The ten that are alive are normal children born at full term. The oldest child is now 23 months, and the youngest is 8 months old. Their development in a nursery, isolated from their mothers, has been normal. Repeated physical examinations have shown no evidence of tuberculosis. Repeated intracutaneous tests with 10 mg. of tuberculin have been negative. Roentgenograms of the chest are normal. In the four infants who died, death occurred from twelve to twenty-eight days after birth. In no instance was there any evidence of tuberculosis. Repeated physical examinations, roentgenologic studies and intracutaneous tests with 10 mg. of tuberculin were negative. Cultures of blood taken from the heart post mortem and of specimens from the lungs, liver and spleen were negative for tubercle bacilli. Postmortem examination revealed nontuberculous bronchopneumonia in the case of an infant born at full term who died in twelve days. In the cases of the other three infants the necropsy examination gave negative results, and the cause of death was attributed to prematurity. The duration of gestation was eight months in two of these cases and seven months in the third.

In the cases of the fourteen new-born infants with negative cultures of umbilical blood the placenta was reported to have no evidence of tuberculosis after a routine macroscopic examination and histologic study of a few sections from several areas.

Of the fourteen mothers, nine had advanced pulmonary tuberculosis and five had minimal, nondestructive pulmonary lesions. In the group with advanced lesions, the tuberculous process progressed during the postpartum period and caused the death of five patients within four months. In those with minimal lesions, there was no evidence of progression of the tuberculous process or of the presence of new lesions during the postpartum period. The new-born infants of the mothers with minimal lesions were normal children born at full term, while those of mothers with advanced tuberculosis were born prematurely in four cases and at full term in five. In five mothers with advanced phthisis, specimens of blood were taken before and after labor and cultured for tubercle bacilli. These cultures gave negative results.

SUMMARY

Fifteen new-born infants of tuberculous mothers were studied for evidence of the transmission of tubercle bacilli by way of the umbilical vein.

Cultures of umbilical blood by the Loewenstein method were negative for tubercle bacilli in fourteen cases and positive in one.

In the case in which the culture of umbilical blood was positive, the placenta had a large tuberculous area. The child was born prematurely at 7 months, and he died three hours after birth with no demonstrable lesions on postmortem examination. A culture of the heart blood was strongly positive for tubercle bacilli. The mother died of tuberculosis eighteen hours after delivery.

In the fourteen cases in which cultures of umbilical blood gave negative results, the placentas were normal on routine macroscopic examination and on microscopic study of several sections. The newborn infants in this group showed no evidence of tuberculosis. Four died within one month, and cultures of the heart blood and of specimens from the liver, spleen and lungs were negative for tubercle bacilli. Ten are alive and normal, as shown by repeated roentgenograms of the chest and results of intracutaneous tests with 10 mg. of tuberculin. Of the fourteen mothers in this group, nine had advanced pulmonary tuberculosis, and five had minimal, nondestructive lesions. The tuberculous process in those mothers with advanced phthisis progressed during the postpartum period and caused death in five instances. Those with minimal lesions showed no progression after labor.

Cultures of blood taken before and after labor from five mothers with advanced pulmonary tuberculosis were negative for tubercle bacilli by the Loewenstein method.

Dr. Oscar Auerbach, pathologist of Sea View Hospital, performed the necropsies and examined the placentas.

COARCTATION OF THE AORTA

REPORT OF THREE CASES

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I wish to report three cases of coarctation of the aorta that presented an interesting variety of detail both clinically and at necropsy.

REPORT OF CASES

CASE 1.—A boy died twenty-one and one-half hours after birth. Delivery was normal. The baby was blue, and it did not breathe for ten minutes after birth. It remained blue up to the time of death. Birth was said to be five weeks premature although the weight was 7 pounds and 3 ounces (3,260.04 Gm.) and the body length was 20½ inches (52 cm.). A murmur was heard over the precordium which was thought to be systolic. The mother had five children living and well; her family history was irrelevant.

At necropsy the face was very cyanotic. The lips were blue and dry. The conjunctivae were congested. When the thorax was opened the pericardium and its contents were found to occupy practically the entire visible thoracic cavity, compressing the lungs laterally, posteriorly and upward. The heart, great vessels and lungs were removed as one specimen. The heart shrank considerably as soon as the vessels were cut, although the heart was at least three times the normal size after this shrinkage. Immediately beyond the origin of the left subclavian artery the aorta narrowed to an atrophic remnant and continued so to the junction of the ductus arteriosus with the descending aorta (fig. 1). This atrophic remnant admitted only the point of a dissecting needle. It was 3 mm. in length. The aorta was of about normal caliber up to the origin of the left common carotid artery, from which point it was about the caliber of the left subclavian artery up to the point of origin of the latter vessel; immediately after this the marked stenosis began. The ductus arteriosus was patent, the pulmonary artery supplying the descending aorta through the patent ductus and the three structures forming a continuous tube of practically uniform caliber. The internal diameter measured at the junction of the ductus with the descending aorta was 4 mm. The right atrium and ventricle were much hypertrophied while the left atrium, in contrast, was extremely small; the left ventricle more nearly approached the normal size. The right ventricle was about double the capacity of the left. Its walls were 5 mm. thick, equal to that of the left. The capacity of the left atrium was estimated at from 1 to 2 cc.; that of the right, at 10 cc. The interventricular septum was intact. The ostium primum was closed. The foramen ovale was patent and measured 4 by 2 mm. The lungs appeared atelectatic both externally and on section. Microscopically the lungs showed partial atelectasis; there were many mononuclear cells bearing brass-yellow pigment.

CASE 2.—A boy born spontaneously at full term was admitted to the hospital when 6 weeks old because of vomiting, failure to gain weight and attacks of

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cyanosis. The child appeared emaciated and dehydrated. No cardiac murmurs were elicited. The upper part of the sternum showed some flattening, while the chest below the third and fourth ribs appeared to bulge somewhat. Occasional cyanotic attacks were observed which cleared up when the baby was held erect. One week after admission to the hospital a roentgen treatment was given for enlarged thymus that was thought to be present. The child continued to have occasional attacks of dyspnea and cyanosis, but these were thought to be less marked following roentgen treatment, and, as the child's condition was thought to be improving, the case was reported by Denney [1] as one of persistent thymus with an apparently favorable result following roentgen treatment. There was no continued gain in weight, however. Finally the Cheyne-Stokes type of respiration developed, and the baby died six weeks after admission at the age of 3 months.

At necropsy the thymus was found to be atrophied, weighing 3 Gm. The heart appeared markedly enlarged and compressed the left lung. It weighed 43 Gm. The right and left atria emptied into a common ventricle. The right ventricle was represented by the infundibulum only. This was 2 cm. in length and 5 mm. in width at the pulmonary orifice; it decreased in width toward its apical end, where it communicated with the common ventricle through an opening 2 mm.

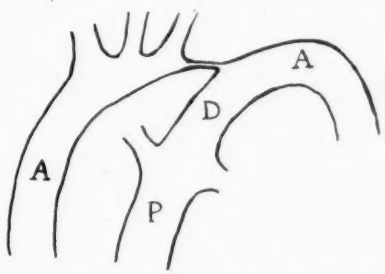

Fig. 1 (case 1).—Diagram of the great vessels, with *A* indicating the ascending and descending aorta, *P*, the pulmonary artery, and *D*, the ductus arteriosus.

in diameter. The foramen ovale was closed. The ascending aorta was greatly dilated, measuring 2 cm. in diameter where it left the common ventricle. Complete coarctation of the aorta existed beyond the origin of the left subclavian artery. The pulmonary artery was continuous with the descending aorta through the ductus arteriosus. The ductus was 3 mm. in diameter and the descending aorta 6 mm. Microscopically the lungs showed some atelectasis, compensatory emphysema and interstitial pneumonitis.

Case 3.—A boy aged 4 months was admitted to the hospital in a cyanotic condition. The child had suffered from diarrhea for a few days previous to admission. The diarrhea ceased, but the cyanosis continued. The patient had had previous attacks of cyanosis but had been healthy otherwise. The temperature was normal on admission, the pulse rate was 145, and the respiratory rate was 50. The baby was well developed and not emaciated or dehydrated. Physical examination otherwise gave negative results. The red blood cell count was 4,200,000, the white cell count, 14,000, and the hemoglobin content, 80 per cent (Dare). The condition appeared to improve slightly and the baby slept, but he wakened crying, became cyanotic again and died within twenty-four hours after admission.

1. Denney, W. L.: Persistent Thymus, Canad. M. A. J. **17**:89 (Jan.) 1927.

The body was that of a well nourished infant 25¼ inches (64.1 cm.) in length. There was a slight ashen-gray hue to the face, and the lips were bluish pink. The finger-tips were of normal shape. There was a considerable quantity of pale straw-colored fluid in the abdomen. The heart occupied practically the whole length and width of the chest. The apex touched the wall of the chest on the left side opposite the seventh rib. The thymus occupied the small portion of the thoracic cavity above the heart. A small portion of the upper lobe of the right lung was overlapping the lower part of the right auricle, and a small portion of the anterior border lay between the upper part of the right auricle and the wall of the chest; the remainder of both lungs was hidden behind the heart. The heart was lying transversely in the cavity and measured 9.5 cm. across (from the apex to the right border of the right auricle) and 6 cm. from above downward. The right border of the heart was 1 cm. from the wall of the chest on the right at its closest point. The heart weighed approximately 85 Gm. (The heart and lungs were removed as one specimen.) The aorta was constricted just proximal to its junction with the ductus arteriosus (fig. 2). The internal diameter proximal to the constriction was 6 mm., at the constriction, 3 mm., and distal to the constriction, 4.5 mm. The internal diameter of the innominate artery was

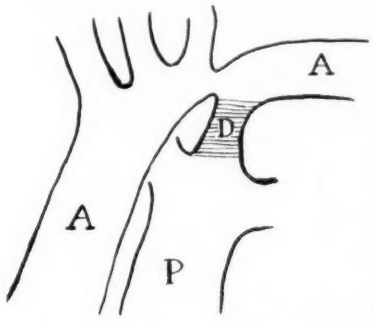

Fig. 2 (case 3).—Diagram of the great vessels, with *A* indicating the ascending and descending aorta, *P*, the pulmonary artery, and *D*, the ductus arteriosus, nonpatent.

3 mm., that is, equal to that of the constricted portion of the aorta. The ductus arteriosus was not patent although it measured 4 mm. in the outside diameter. The heart shrank quickly and markedly when the blood vessels were cut. The wall of the left ventricle was 7 mm. in thickness, and the cavity was greatly dilated. The right atrium and the right ventricle were likewise much dilated. The foramen ovale showed a slight slitlike opening less than 1 mm. in width and 3 mm. in length. There was an opening in the pars membranacea of the interventricular septum, which with slight difficulty admitted a glass rod 8 mm. in diameter. Most of the upper lobe of each lung, the middle lobe of the right lung and part of the lower lobe of the left lung were more or less atelectatic. The brain showed some edema.

Summary of Cases.—Of three cases of coarctation of the aorta between the origin of the left subclavian artery and the ductus arteriosus two were complete and one moderate. The ductus arteriosus was patent in both cases of complete coarctation and closed in the one of moderate coarctation. There was a small opening in the interventricular septum in the latter case, while there was complete absence of an interventricular

septum in the second case, and no cardiac anomalies were evident in the first case. In the case in which the least hypertrophy was noted serious obstruction was evident in both the aortic and the pulmonary channel. Even in this case the heart weighed 43 Gm. The extreme degree of hypertrophy and dilatation in the other two cases was remarkable in view of the fact that this is said to be an unusual finding in cases of infantile coarctation.[2] The hypertrophy of the right ventricle in the first case must obviously have been antenatal since the baby lived less than twenty-four hours.

Comment on Cases.—It is convenient to consider the cause of the cyanosis and the cause of death together in the individual cases. It is evident that the hypertrophy in case 1 must have taken place before birth and that, even if part of the dilatation took place after birth, the size of the heart was sufficient at birth to compress the lungs and interfere more or less with the aeration of the blood flowing through them. The hypertrophy of the right ventricle can be accounted for, in whole or in part, by the fact that it was called on to do all the work of supplying blood to the descending aorta, a task that is ordinarily shared by the left ventricle. The lack of sufficient expansion of the lungs and venous stasis due to obstruction in the compressed lung with consequent cardiac dilatation apparently formed a vicious circle that accounted for the cyanosis and probably was the cause of death.

In case 2 there was obstruction in the pulmonary channel (at the infundibulum) as well as in the aorta, and the heart, especially when enfeebled by malnutrition, was unable to supply sufficient blood to the lungs in response to the extra demand in times of special effort, such as during crying. In addition, in this case the arterial and venous blood were constantly being mixed in the single ventricle so that a certain degree of suboxygenation must have existed all the time, making it easier for any additional factor to raise the carbon dioxide-hemoglobin content of the blood up to the cyanotic level. Apparently posture was, at times, a factor in the production of the cyanosis in this case. Death was probably due to marasmus.

In case 3 the ductus arteriosus may possibly have been patent to some degree until a short time before death; and its final closure, whenever it took place, no doubt added to the burden of the cardiac mechanism. The size of the heart not only decreased the space available for expansion of the lung but produced actual atelectasis. My conception of the pathologic physiology of the fatal illness is as follows: In response to the factor that produced the diarrhea there was likely a demand for an increased cardiac and respiratory activity. Neither the

2. Abbott, Maud E., in Osler, W., and McCrae, T.: Modern Medicine, Philadelphia, Lea & Febiger, 1915, vol. 4, p. 420.

lungs nor the heart was able to meet the demand, and the heart responded by dilatation in the presence of the aortic obstruction, further embarrassing the lungs. The venous stasis and the atelectasis together further reduced the oxygenation, allowing the carbon dioxide-hemoglobin content to accumulate up to the cyanotic level. Finally, the extremely dilated heart became unable to contract.

COMMENT

The separation of the cases of coarctation into infantile and adult types is useful because it corresponds to a difference in clinical course correlated to an anatomic difference. The real value of the classification has possibly been obscured to some extent by the controversy over the theoretical contention that the adult type is acquired, whereas it is probably congenital,[3] as is the infantile type. While infants with the latter type usually die in infancy, patients with the adult type frequently live to adult life or even old age (one patient was 92) and have been known to engage for years in heavy manual labor or athletics or to give birth to several children without showing cardiovascular symptoms. Cases in which the constriction is opposite to or distal to the entrance of the ductus arteriosus are of the adult type. It is significant that in such cases there is interference with the free flow of blood into the descending aorta both by way of the ductus arteriosus and by way of the aortic arch, whereas in cases of the infantile type, with the constriction proximal to the entrance of the ductus, the flow of blood through one of these channels remains unimpaired.

I should like to suggest that this difference in mechanical effect due to the difference in the site of the stricture is the factor that determines the amazing difference in the clinical course and prognosis between the infantile and the adult type. When the constriction is between the origin of the left subclavian artery and the ductus arteriosus the left ventricle fails to supply its share of blood to the descending aorta, and yet an adequate circulation can be carried on in the fetus by the transfer of extra work to the right ventricle without the establishment of a collateral circulation. In other words, there is little or no incentive to the establishment of a collateral circulation until after birth, and the infant is ill-fitted, indeed often incompetent, to establish a circulation of the extra-uterine type adequate for ordinary needs, and much less able to meet the unusual strains of postnatal life. On the other hand, when the constriction is at or beyond the ductus arteriosus it is imperative that an adequate collateral circulation be established in early embryonal

3. Abbott, Maud E.: Coarctation of the Aorta of the Adult Type, Am. Heart J. **3**:392, 1928. (*b*) Blackford, M. L.: Coarctation of the Aorta, Arch. Int. Med. **41**:702 (May) 1928. (*c*) Evans, W.: Congenital Stenosis (Coarctation), Atresia and Interruption of the Aortic Arch, Quart. J. Med. **2**:1 (Jan.) 1933.

life if the fetus is to survive, even in utero, since survival is impossible without a sufficient flow of blood into the descending aorta. Owing to this forced establishment of a collateral circulation in fetal life the infant is much better equipped to meet successfully the strains put on it in early and later postnatal life.

There are cases of the adult type of coarctation in which arterial channels normally obliterated in early fetal life have been retained, as if this were part of the response to such a demand. Such a case has been reported by Blackford,[3b] in which there was a large persistent right dorsal aorta. Blackford pointed out that if a collateral circulation is established in early embryonic life little disturbance may result from the coarctation.

If the explanation that I have suggested is valid no case should be classified as being of the adult type unless the constriction is so situated as to justify the conclusion that the flow of blood through the ductus arteriosus into the descending aorta is, or was, obstructed during fetal life. This would apply particularly to that small group with the constriction "just above," "just proximal to" or "near" the entrance of the ductus arteriosus and classified as adult on the basis of the type of the constriction.[4]

After all, the type of constriction, whether sudden or diffuse, may depend on the presence of certain modifying factors rather than on the presence of a fundamentally different mechanism. Further, there is no longer a need to postulate a different mechanism because of the position of the constriction in the adult type, since Congdon[5] has shown that the insertion of the ductus arteriosus is not constant and that it may be inserted into the isthmus in some cases rather than at its distal limit. Thus, constrictions distal to the insertion of the ductus may still be constrictions of the isthmus.[3b]

Thompson[6] and others have said that the clinical interest of the infantile type of coarctation is slight, that it is practically impossible to make the diagnosis during life and that it does not matter since the subjects are doomed to die in infancy or early childhood. Evans[3c] expressed the opinion that the condition can be diagnosed by finding the signs of a patent ductus arteriosus. These he described as a rough systolic murmur heard best in the pulmonary area, the pulmonary second sound being still audible or accentuated, and a thrill which may or may not be present. At any rate, these cases are bound to present an interesting problem in diagnosis to the pediatrician, as case 2 in this

4. Hamilton, W. F., and Abbott, Maud E.: Coarctation of the Aorta of the Adult Type, Am. Heart J. **3**:381, 1928. Abbott,[2, 3a] Blackford.[3b]

5. Congdon, E. D.: Contrib. Embryol. **14**:47, 1922.

6. Thompson, J., in Christian, H. A., and McKenzie, S.: Oxford Medicine, New York, Oxford University Press, 1920, vol. 2, p. 371.

series illustrates. Case 3 was also very puzzling to both the general practitioner and the pediatrician.

A rather keen interest in the adult type of coarctation is indicated by the number of articles which have appeared in the recent literature and by the fact that the diagnosis is apparently being made with increasing frequency. The diagnosis has been made clinically and confirmed at necropsy in more than twenty cases and has been made on adequate clinical evidence in at least fifty cases more.[3b] The adult type has been found at necropsy in two hundred cases or more. The incidence at necropsy of both types combined seems to be about 1 in 1,000.[3c] Some clinical observers have remarked on the ease with which the diagnosis can often be made and have expressed surprise that it is so frequently missed. One case is on record in which the diagnosis was missed clinically but was made by the pathologist when he turned the patient over to look at the back during the preliminary examination. The clinical signs have been well described and discussed by King,[7] Blackford [3b] and Blumgart, Lawrence and Erstene.[8] The outstanding points clinically are: high blood pressure in the arms as contrasted with relatively low pressure in the legs, diminution and retardation of the arterial pulse in the legs and the presence of an extensive collateral circulation to be looked for particularly in the interscapular region and in the intercostal area, where it is frequently shown by erosion at the lower borders of the ribs. The main causes of death in the adult type are myocardial failure, rupture of the aorta (including dissecting aneurysm) and cerebral hemorrhage.

SUMMARY

Three cases of coarctation of the aorta of the infantile type have been presented with comments on the pathologic physiology.

It has been suggested that the better prognosis in the adult type of coarctation is due to the position of the constriction, forcing the establishment of a collateral circulation during early fetal life at a time when, incidentally, it can be most readily established.

It has been suggested that the classification of a given case as of the infantile or of the adult type should depend on the ability or inability of the constriction to produce obstruction of the flow of blood from the ductus arteriosus into the descending aorta in fetal life, owing to its position.

Comment has been made on the diagnosis and clinical and postmortem incidence.

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7. King, J. T.: Stenosis of the Isthmus (Coarctation) of the Aorta and Its Diagnosis During Life, Arch. Int. Med. **38**:69 (July) 1926.

8. Blumgart, H.; Lawrence, J. H., and Erstene, A. C.: The Dynamics of the Circulation in Coarctation (Stenosis of the Isthmus) of the Aorta of the Adult Type, Arch. Int. Med. **47**:806 (May) 1931.

MALDEVELOPMENT AND MALDESCENT OF THE TESTES

REPORT OF TREATMENT WITH THE ANTERIOR PITUITARY-LIKE GONADOTROPIC HORMONE FROM THE URINE OF PREGNANT WOMEN

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In 1932, Engle [1] demonstrated that the use of an extract of the anterior lobe of the pituitary gland or of the urine of pregnant women in immature rats and monkeys caused a definite increase in the size of the testes. This was due to an increase in tubular growth and in interstitial cellular mass. However, no change in gametogenesis was noted by him in his experiment. He suggested the possible application of this phenomena to the human being.

As a result of Engle's work, Goldman and Stern [2] proceeded with a study on human beings and demonstrated the effectiveness of the anterior pituitary-like gonadotropic hormone on the undescended testes of two adolescent boys. B. Schapiro [3] had obtained good results in a group of males presenting hypoplastic and undescended testes by the use of a commercial gonadotropic preparation.[4]

Subsequently, Brosius and Schaffer [5] produced spermatogenesis in a man whose testes had become bilaterally atrophied because of orchitis complicating mumps.

Presented before the New York Endocrinological Society, Jan. 23, 1935.

Presented at the Nineteenth Annual Convention of the Association for the Study of Internal Secretions at Atlantic City, N. J., June 11, 1935.

From the Endocrine Clinics of the Department of Pediatrics, the New York University Medical College, the Children's Medical Service of the Third Medical Division, Bellevue Hospital and the Beth-El Hospital.

1. Engle, E. T.: The Action of Extracts of Anterior Pituitary and of Pregnancy Urine on the Testes of Immature Rats and Monkeys, Endocrinology **16:** 506 (Sept.-Oct.) 1932; Experimentally Induced Descent of the Testis in the Macacus Monkey by Hormones from the Anterior Pituitary and Pregnancy Urine, ibid. **16:**513 (Sept.-Oct.) 1932.

2. Goldman, A., and Stern, A.: Treatment of Undescended Testis by Injection of Prolan, New York State J. Med. **33:**1095 (Sept. 15) 1933.

3. Schapiro, B.: Kann man mit Hypophysenvorderlappen den unterentwickelten männlichen Genitalapparat beim Menschen zum Wachstum anregen?, Deutsche med. Wchnschr. **56:**1605 (Sept. 19) 1930; Ist der Kryptorchismus chirurgish oder hormonal zu behandeln? Deutsche med. Wchnschr. **57:**718 (April 24) 1931.

4. The preparation used was praehormon (Promonta).

5. Brosius, W. L., and Schaffer, R. L.: Spermatogenesis Following Therapy with the Gonad Stimulating Extract from the Urine of Pregnancy, J. A. M. A. **101:**1227 (Oct. 14) 1933.

Sexton [6] in a series of patients showed definitely the effectiveness of the anterior pituitary-like gonadotropic hormone on hypoplastic genitals.

At this point, I wish to contribute my findings in a group of fourteen patients with hypoplastic genitals who were treated with the anterior pituitary-like gonadotropic hormone from the urine of pregnant women (and with the anterior pituitary growth hormone). The reports of the cases (table) and observations are herewith presented.

COMMENT

In all the patients of this series who were treated over a sufficient period of time with anterior pituitary-like gonadotropic hormone, effective results on the genital system were obtained. In seven of

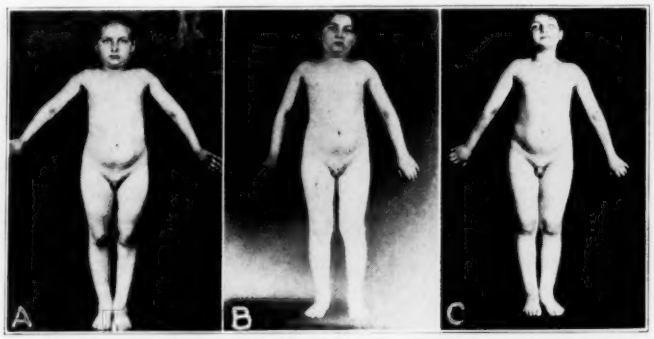

Fig. 1 (case 1).—*A* shows J. S., a patient with hypothyroidism, at the age of 7½ years before treatment with thyroid extract; *B*, at the age of 8½, after one year of treatment with thyroid extract and four months of treatment with extract of anterior pituitary-like hormone; *C*, at the age of 8¾, after eight months of treatment with anterior pituitary-like hormone (33,375 rat units).

eight patients with unilaterally or bilaterally undescended testes there was some increase in size and descent while in the other patients with hypoplastic testes there was a double or triple increase in size.

In case 2 one testis was not brought down, although the other testis and the secondary sex accessories were greatly stimulated. The possibility of a mechanical obstruction or a congenital absence of the testis must be considered.

6. Sexton, D. L.: Treatment of Sexual Underdevelopment in the Human Male with the Anterior Pituitary-Like Hormone of Urine of Pregnancy, Endocrinology **18**:47 (Jan.-Feb.) 1934.

The first apparent sign of the effectiveness of the therapy was usually a blushing or pinkish coloration of the scrotum and often of the penis. Then the scrotum tended to become edematous, relaxed and wrinkled or rugose, and the "labia-like" or "raphe-like" scrotum began to pucker out. With the enlargement of the scrotum, one usually could notice an increase in the size of the testes and, later, of the penis. There appeared blond, fuzzy pubic hairs, which later became pigmented, more numerous and longer.

This progression of development was noticed even in the younger children. It also was found that the size of the penis could be

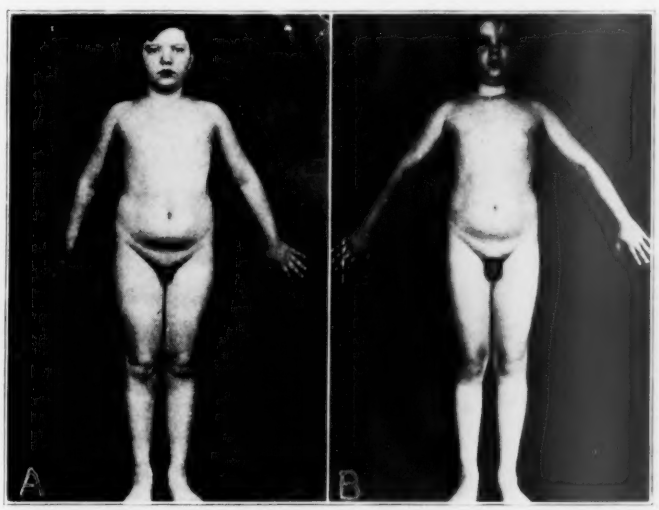

Fig. 2 (case 2).—*A* shows A. B. at the age of 9 years, before treatment; *B*, at the age of 10 years, after treatment with anterior pituitary-like hormone (45,200 rat units in ten months).

increased to adolescent proportions. This occurred in a patient (case 2) aged 10½ years who received a total of 45,200 rat units in ten months, the largest amount given in our series. The treatment in this case was prolonged with the hope of causing a change in the apparently absent testis. As was stated previously, such a change did not occur, and the possibility of a mechanical obstruction or of congenital absence of the testis was suggested. Also, in a patient aged 13½ (case 11) a nocturnal emission of semen was encountered for the first time.

The following findings are of interest: 1. It was necessary to administer a large quantity of hormone before beneficial effects were evident and a larger number of total rat units before effectual results

Observations on Fourteen Boys Treated with the Gonadotropic Anterior Pituitary-Like Hormone for Maldevelopment and Maldescent of the Testes *

Patient	Age, Years	Type and Appearance	Basal Metabolic Rate, per Cent	Laboratory Data	Roentgenograms: Sella Thymus	Roentgenograms: Osseous Development	Genital Development Before Each Corresponding Treatment	Treatment	Genital Response
1 J. S.	8¾	Hypothyroid; eunuchoid; normal height; obese +20	—14.0	Chol., 105; Ca, 13.2; Wass., neg.; urine normal	Normal	Retarded	1. Testes not felt before thyroid therapy	1. Thyroid therapy for 1 year previous to A.P.H. treatment	1. Pea-sized testes high up in canal which can be brought down to high scrotal position
					Normal	.....	2. Hypoplastic, undescended pea-sized testes in canal; scrotum and penis small	2. A.P.H., 0.5 to 1.5 cc. 3 times a week, then daily; 116 injections in 10 months (33,375 rat units)	2. Testes tripled, in scrotum; scrotum filled out, pigmented; penis increased to 2⅛ in.; prostate undefined; right epididymis more prominent
2 A. B.	10	Hypothyroid; normal proportions; overgrown +3.3; obese +37	—23.5	Urine, normal with faint trace of albumin	Normal	Slightly retarded	1. Right testis, pea-sized, in midscrotum; left testis not felt; penis small	1. Thyroid therapy for 1½ years	1. Right testis increased, in scrotum; left testis not felt
					Normal	.....	.....	2. A.P.H., 1 to 1.5 cc. 3 times a week, then daily; 141 injections in 10 months (45,200 rat units)	8. Right testis tripled; left not felt; penis longer and thicker, 2½ in.; scrotum well formed; many long black pubic hairs; right lobe of prostate enlarged to 14 year old size; left lobe undefined; epididymis good size
3 M. L.	8½	Hypothyroid; eunuchoid; normal height; overweight +8	—18.0	Urine, faint trace of albumin and occasional hyaline cast	Normal	Slightly retarded	1. Pea-sized testes in scrotum; scrotum relaxed; penis medium-sized	1. Thyroid therapy for 7 weeks	1. No change
					Normal	.....	.....	2. A.P.H., 1 to 1.5 cc. 3 times a week, then daily; 135 injections in 10 months (39,250 rat units)	2. Testes tripled, in scrotum; scrotum enlarged; many black pubic hairs; penis 2½ in. (6.35 cm.); prostate undefined; right epididymis prominent
4 P. L.	7¼	Hypothyroid; eunuchoid; normal height; obese +16	Uncooperative	Chol., 85; Ca, 12.4; Wass., neg.	Normal	Retarded	1. Left testis size of a small pea, in scrotum; right testis not felt; penis small and buried in mons fat	1. A.P.H., 1 to 1.5 cc. 3 times a week, then daily; 66 injections in 10 months (20,000 rat units)	1. Left testis doubled in scrotum; right testis increased, high in scrotum, with thickening of spermatic cord; scrotum enlarged and congested; penis 1½ in. and slightly buried in mons fat; prostate undefined; white fuzzy pubic hair
5 M. C.	12¼	Hypothyroid; eunuchoid; short —2.9; overweight +9.6	—8.5	Urine, faint trace of albumin; slight meatitis at end of treatment	Small	Retarded; poor structure	1. Hypoplastic testes in scrotum, tending to retract; penis buried in mons fat	1. A.P.H., 1 to 1.5 cc. 3 times a week, then daily; 78 injections in 9 months (21,375 rat units)	1. Testes tripled, in scrotum; scrotum increased; penis 1¾ in.; many long black pubic hairs
					Normal				

6 J. H.	8	Hypothyroid; normal proportions; overgrown +2.3; obese +22	—15.8	(Before thyroid treatment) N.P.N., 25.5; Uric ac., 2.8; Chol., 210; Chl., 462; Ca, 12	Normal	Retarded	1. Small testes in canal; penis small 2. Testes small in high scrotum; penis small, buried in mons fat	1. Thyroid therapy for 18 months 2. A.P.G., 1 cc. and A.P.H., 0.33 cc.; 64 injections in 7 months (5,312 rat units) 3. A.P.H., 1 to 1.5 cc. daily, then 3 times a week; 26 injections in 1½ months (total, 14,666 rat units in 90 injections)	1. Slight descent of testes; size slightly increased 8. No apparent change 3. Testes doubled, in scrotum; left testis as large as kidney bean; right slightly smaller; scrotum markedly filled out; penis increased to 1½ in., not buried; no hair; prostate undefined; epididymis felt but not enlarged
7 D. K.	8½	Hypothyroid; normal proportions; overgrown +4.8; obese +40	—3.3	.....	Small	Slightly retarded	1. Hypoplastic left testis in midscrotum; right testis not felt after several attempts, although 6 months before it was felt by another physician high in canal	1. A.P.G., 1 cc.; 22 injections in 2 months 2. A.P.H., 0.5 to 1 cc. 3 times a week; 9 injections (1,875 rat units) 3. A.P.H., 1 to 1.5 cc. 3 times a week, then daily; 25 injections in 3 months (total 8,375 rat units)	1. Left testis not changed; right felt for first time, high in canal; very small and could not be brought down (findings 2 months after treatment with A.P.G.) 2. Both testes equal in size, in scrotum; right retracted; no pubic hair 3. Left testis doubled, in scrotum; right testis smaller, in midscrotum; scrotum relaxing; penis 1½ in.; prostate undefined; epididymis small
8 M. W.	10¼	Hypothyroid; eunuchoid; overgrown +3.8; obese +43	—11.0	Urine, normal	Normal	Retarded	1. Left testis size of a large pea; right slightly larger and retracted; penis 1¼ in.	1. A.P.G., 1 cc., and A.P.H., 0.33 cc., 3 times a week for 25 injections	1. No apparent change
					Normal	.....	.....	2. A.P.G., 1 cc., and A.P.H., 0.5 cc., 3 times a week for 38 injections 3. A.P.H., 1 to 1.5 cc., 3 times a week, then daily; 65 injections in 10 months (26,626 rat units)	2. No apparent change 3. Left testis doubled, in scrotum; right larger, in midscrotum; scrotum relaxed, enlarged; prostate undefined; penis 1⅝ in.
9 M. S.	11¼	A.G.D.; eunuchoid; overgrown +2.3; obese +69	—3.0	Urine, normal	Bridged	Normal	1. Marble-sized testes in canal; scrotum labia-like and small; penis small and buried in mons fat; no pubic hair	1. A.P.H., 0.5 to 2 cc. 2 to 4 times a week; 80 injections in 9 months (22,000 rat units)	7. Testes larger, descended to high in scrotum; scrotum relaxed and well formed; penis larger; many black pubic hairs

* All anthropometric readings are taken from Engelbach, W.: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 1. The size of the testes was obtained by palpation, and approximate diagrams were recorded. The penis was measured in the flaccid state. The plus or minus sign indicates the number of pounds or inches above or below the optimal for age.

A.G.D. indicates adiposogenital dystrophy; A.P.H., anterior pituitary-like gonadotropic hormone (250 rat units per cc.); A.P.G., anterior pituitary growth hormone; Chol., cholesterol; Ca, calcium; Wass., Wassermann; N.P.N., nonprotein nitrogen; Uric ac., uric acid; Chl., chlorides.

Observations on Fourteen Boys Treated with the Gonadotropic Anterior Pituitary-Like Hormone for Maldevelopment and Maldescent of the Testes—Continued*

Patient	Age, Years	Type and Appearance	Basal Metabolic Rate, per Cent	Laboratory Data	Roentgenograms: Sella Thymus	Roentgenograms: Osseous Development	Genital Development Before Each Corresponding Treatment	Treatment	Genital Response
10 N. R.	11	A.G.D.; normal proportions; normal height; obese +30	+8.0	.....	Normal	Normal	1. Pea-sized testes; penis buried in mons fat	1. Period of observation, 20 months	1. Testes slightly increased to size of a small almond
							2. Scrotum small; penis medium size; buried in mons fat	2. A.P.G., 1 cc., and A.P.H., 0.33 cc., 3 times a week; 20 injections	2. No apparent change
								3. A.P.G., 1 cc., and A.P.H., 0.5 cc., 3 times a week for 18 injections (3,916 rat units); discontinued	3. Small testes in scrotum; left slightly larger than right; slight fuzz of white hair
11 L. W.	13½	A.G.D.; eunuchoid; overgrown +2.1; obese +31	−18.0	.....	Normal	Normal	1. Testes small, in midscrotum; scrotum labia-like; no pubic hair; penis small	1. A.P.H., 0.5 to 2 cc. 2 or 3 times a week; 75 injections in 9 months (18,000 rat units)	1. Testes increased, in scrotum; scrotum well formed; penis 2 in.; many black pubic hairs; nocturnal emission
12 H. L.	6	A.G.D.; eunuchoid; normal height; obese +20	Uncooperative	Urine, faint trace of albumin	Normal	Normal	1. Left testis the size of a small pea, in midscrotum; right larger, in canal; scrotum tense; penis small	1. Thyroid therapy for 3 weeks, ½ year before	1. No apparent change
					Normal	.....	.....	2. A.P.G., 1 cc., and A.P.H., 0.33 cc., 3 times a week for 20 injections	2. No apparent change
								3. A.P.G., 1 cc., and A.P.H., 0.5 cc. 3 times a week for 64 injections (10,000 rat units)	3. Right testis, slightly increased; scrotum rugose; penis 1½ in.
								4. A.P.H., 1 to 1.5 cc. daily, then 3 times a week; 47 injections (total, 21,000 rat units in 10 months)	4. Testes doubled, in scrotum; scrotum relaxed; prostate undefined; no pubic hair
13 L. S.	9½	A.G.D.; eunuchoid; overgrown +4; obese +48	−9.3	Urine, faint trace of albumin	Normal Normal	Normal	1. Small kidney bean sized testes in scrotum	1. A.P.G., 1 cc., and A.P.H., 0.33 cc., 8 injections in 1 month; discontinued	1. No apparent change
14 D. G.	11¾	A.G.D.; eunuchoid; normal height; obese +38	−22.0	.....	Normal	Normal	1. Right testis the size of a large almond, left smaller; both in scrotum; penis small	1. A.P.G, 1 cc., 3 times a week; 36 injections in 3 months; discontinued	1. No apparent change

were obtained. 2. The response was slow, and very little change could be observed during the first few months of therapy. 3. The age of the children was apparently of no consequence in the final result of the treatment, although those closer to puberty showed a more rapid response. The most efficacious dosage was found to be a large dose of anterior pituitary-like gonadotropic hormone from the urine of pregnant women (250 rat units) given from three to five times a week until there was a genital response, and then the same amount given three times a week. 5. The use of the anterior pituitary growth hormone in conjunction with anterior pituitary-like gonadotropic hormone apparently did not detract from, nor did it enhance, the effectiveness of the latter hormone on the genitals.

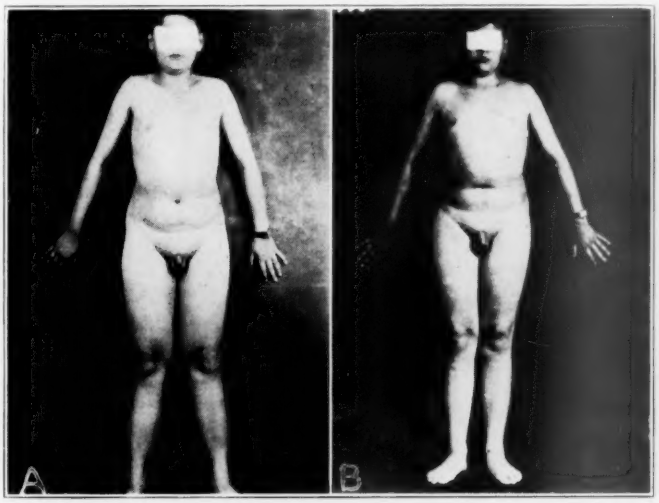

Fig. 3 (case 11).—*A* shows L. W. at the age of 13, before treatment; *B*, at the age of 13½, after treatment with 18,000 rat units of anterior pituitary-like hormone.

Although this series of patients with hypoplastic genitals is small, and therefore one cannot make definite classifications or reach definite conclusions, there appeared in this series two predominant types of persons: (1) those with adiposogenital dystrophy, showing obesity, genital dystrophy, height usually accelerated above the average normal, eunuchoid body measurements, normal osseous development and a basal metabolic rate on the minus side; (2) those with mild or masked hypothyroidism, showing developmental retardation, frequent obesity, a lowered basal metabolic rate, hypoplastic genitals, usually normal body proportions, although the height was often below the average normal, and, particularly, varying degrees of retardation of osseous development.

The condition of the patients in group 1 (and of some in group 2) is called Fröhlich's syndrome, although there seems to be no apparent association of this condition with the neoplastic pathologic condition of the pituitary region found in the true Fröhlich syndrome. Neoplastic involvement of the anterior lobe of the pituitary and the neighboring area, although producing genital atrophy and occasionally obesity, usually causes proportionate dwarfism in a child rather than overgrowth. It is, therefore, my belief that in this series of patients (group 1) the adiposogenital dystrophy was due not to pituitary disturbance but rather to primary hypogonadism presenting a subsequent train of symptoms simulating those of incomplete castration.

The patients in group 2, with mild or masked hypothyroidism, were classified as such, because in addition to the symptoms listed for the

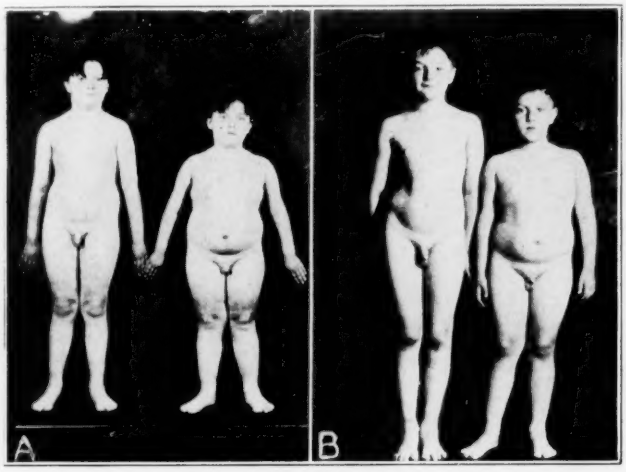

Fig. 4.—*A* shows M. L. (case 3) at the age of 8 and H. L. (case 12) at the age of 5, before treatment; *B*, M. L. at the age of 8½, after treatment with anterior pituitary-like hormone (39,250 rat units), and H. L. at the age of 5½, after treatment with the anterior pituitary growth hormone and with the anterior pituitary-like hormone (21,000 rat units).

patients with adiposogenital dystrophy, they had a history of retardation of general and of osseous development, the latter being evidenced in the centers of ossification and the epiphyseal nuclei. In a previous series of forty patients with a similar condition, I found that 85 per cent of twenty-four boys presented hypoplastic genitals with retardation of general and osseous development.[7] These two gross symptoms, retardation of general and of osseous development, as I have already stated in a

7. Dorff, G. B.: Masked Hypothyroidism in Children: Osseous Development as an Aid in the Diagnosis, J. Pediat. **6**:788 (June) 1935.

previous article,[7] are, I believe, primary manifestations of deficient thyroid function. In every one of the patients whom I previously treated with thyroid extract with good results, I found such retardation.

Consequently, the patients belonging to group 2 (listed in the table) were treated with thyroid, and good results were obtained. Ossification was advanced, the basal metabolic rate was increased, and other effects of thyroid replacement became evident. However, with regard to the genital development under treatment with thyroid the response was mild. At this point, therefore, thyroid medication was discontinued and the anterior pituitary-like gonadotropic hormone was administered. The genitals responded considerably. However, with this definite progress in the development of the genitals there was no longer as much ossification, although in two or three patients there was advance in osseous development similar to that noted after thyroid medication. Generally, however, the process of ossification was slowed and was no longer commensurate with that noted during the period of thyroid therapy. This was also true of the basal metabolic rate, which showed no appreciable rise. These findings confirmed my belief that the thyroid gland was involved, and therefore I put such patients in a separate grouping.

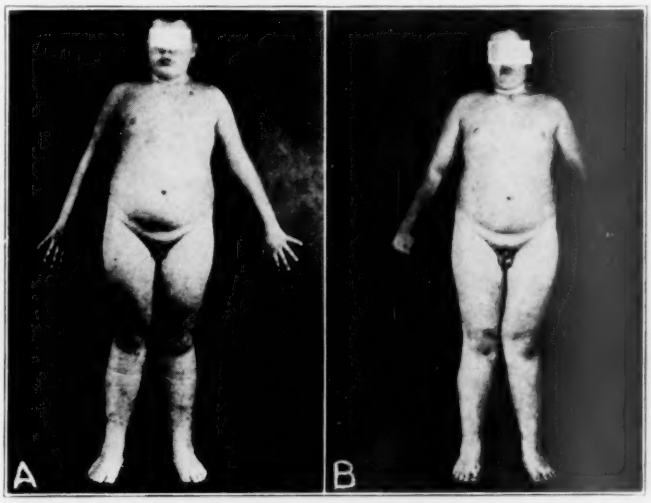

Fig. 5 (case 9).—*A* shows M. S. at the age of 10¾ years, before treatment; *B*, M. S. at the age of 11¼ years, after treatment with 22,000 rat units of anterior pituitary-like hormone.

The definite genital response that occurred in these patients with mild hypothyroidism after injections of the anterior pituitary-like gonadotropic hormone from the urine of pregnant women can be

explained by the fact that the hormone exerts its effect directly on the testes. This has been suggested by Smith and Leonard,[8] who showed that after hypophysectomy the genitals can still be stimulated by the anterior pituitary-like gonadotropic hormone. That the testes play an essential intermediary rôle in the change produced in the pituitary gland and sex accessories was shown by Nelson.[9] His work on experimental cryptorchidism suggested that the testes, the seminal vesicles, the prostate and the anterior lobe of the pituitary gland, which presented changes similar to those after castration, although retarded, after the injection of the urine of pregnant women corrected the "castration" changes in the anterior lobe of the pituitary and the seminal vesicles. However, complete removal of the testes and subsequent injection of the urine of pregnant women did not correct the "castration" changes that occurred in the anterior lobe of the pituitary; neither did it correct the atrophy of the sex accessories. It was apparent to Nelson from the effect on the sex accessories that treatment with the gonadotropic hormone stimulated the production of testicular hormone by some component of the undescended testis, probably the interstitial cells.

Finally, that the anterior pituitary-like gonadotropic hormone from the urine of pregnant women does not stimulate the thyroid gland has been shown histologically, for Hertz and Kranes [10] and Collip [11] experimented with giving injections of the anterior pituitary-like gonadotropic hormone to animals and obtained no such effect on the thyroid glands.

SUMMARY AND CONCLUSIONS

Fourteen boys ranging in age from 6 to 13 years and showing hypoplasia of the genitals in the form of either maldescent or maldevelopment of the testes have been studied and treated.

The anterior pituitary-like gonadotropic hormone of the urine of pregnant women was effective in all the patients in varying degrees,

8. Smith, P. E., and Leonard, S. L.: Responses of the Reproductive System of Hypophysectomized and Normal Rats to Injections of Pregnancy-Urine Extracts: Male, Anat. Rec. **58**:145 (Jan. 25) 1934; Effect of Injecting Pregnancy-Urine Extracts in Hypophysectomized Rats: Male, Proc. Soc. Exper. Biol. & Med. **30**:1246 (June) 1933.

9. Nelson, W. O.: Effect of Gonadotropic Hormone Injections upon the Hypophyses and Sex-Accessories of Experimental Cryptorchid Rats, Proc. Soc. Exper. Biol. & Med. **31**:1192 (June) 1934.

10. Hertz, S., and Kranes, A.: Exhaustion Phenomenon in Thyroid Produced by Pituitary Treatment: Histological Study of Rabbit's Thyroid Under Varying Degrees of Anterior Pituitary Therapy, Endocrinology **18**:415 (May-June) 1934.

11. Collip, J. B.: Some Recent Advances in the Physiology of the Anterior Pituitary, J. Mt. Sinai Hosp. **1**:28 (May-June) 1934.

depending on the total amount of hormone given and on the duration of treatment.

Two types of patients appeared in this series:

1. Those with so-called adiposogenital dystrophy, which, it is felt, was really due to primary hypogonadism. They showed signs and symptoms of adiposity, hypoplasia of the genitals, overgrowth, eunuchoid proportions and normal osseous development, evidenced by the appearance of the carpal centers and the epiphyseal nuclei.

2. Those with mild or masked hypothyroidism, who showed retarded osseous development and hypoplastic testes in addition to other mild symptoms of thyroid deficiency.

Under therapy, in both those with adiposogenital dystrophy due to primary hypogonadism and those with masked hypothyroidism, the following facts became apparent: (1) Hypoplastic testes increase in size (sometimes threefold); (2) undescended testes increase in size and descend from their high positions in the scrotum and canal; (3) testes not felt on careful examination sometimes can be and are developed; (4) the scrotum fills out and progresses toward normal development; (5) the penis enlarges in size and thickness; (6) pubic hair develops; (7) the epididymis and the prostate are stimulated; (8) possibly congenital hernia frequently said to accompany cryptorchidism may correct itself during the process of descent, and (9) the general mental aspect of the patient changes.

A lowered basal metabolic rate, evident in patients with primary hypogonadism and in those with hypothyroidism, will remain low, even after administration of the anterior pituitary-like gonadotropic hormone, although there may be a slight increase. In all the patients of this series with the exception of one, the basal metabolic rate at the onset of treatment was on the minus side; and it is felt that under true basal conditions and on several repetitions of this test there would be still lower minus rates.

Of the eight patients with unilaterally or bilaterally undescended testis all showed a response to the anterior pituitary-like gonadotropic hormone except one, 10½ years old, in whom a mechanical obstruction or congenital absence of the testis was suspected.

I feel fairly safe in saying that if there are no mechanical factors to obstruct descent, good results can be anticipated and obtained in patients with maldeveloped or maldescended testes, regardless of their size or position. Also, there is the possibility of developing an apparently absent testis, and therefore treatment should be given.

Treatment may be started at any time before puberty. However, patients closer to puberty show a more rapid response.

It is believed that the anterior pituitary-like gonadotropic hormone acts directly on the testis, the producer of the testicular hormone, which in turn stimulates the anterior lobe of the pituitary and the sex accessories.

Although thyroid therapy was discontinued during this study, it is thought that it should be given along with the anterior pituitary-like gonadotropic hormone in order to obtain the best results in the patients with mild or masked hypothyroidism.

It is questionable whether the anterior pituitary-like gonadotropic hormone stimulates the thyroid gland.

The concomitant use of the anterior pituitary growth hormone with the anterior pituitary-like gonadotropic hormone from the urine of pregnant women apparently does not hinder, nor does it enhance, the effects of the latter. However, the paucity of patients in this series and the shortness of the period of observation make this statement and the preceeding one conditional and dependent on future study and findings.

Finally, patients with hypoplastic and undescended testes should not be submitted to surgical procedures until a course of intensive treatment with the anterior pituitary-like gonadotropic hormone has been instituted for one year without success.

My attention has been called to a recent article [12] in which the authors stated that when the anterior pituitary-like gonadotropic hormone (7,000 to 22,000 rat units) was injected into monkeys bilateral enlargement of the breast occurred, provided the testes were present.

In none of the patients in the present series with hypoplastic and undescended testes who were given anterior pituitary-like gonadotropic hormone in large doses was any unusual enlargement of the breasts detected. In fact, some of the originally enlarged breasts seemed to flatten, particularly in those patients who lost weight during treatment.

1176 Eastern Parkway.

12. Geschickter, C. F.; Lewis, D., and Hartman, C. G.: Tumors of the Breast Related to the Oestrin Hormone, Am. J. Cancer **21**:828 (Aug.) 1934.

APPENDICULAR FORM OF BACILLARY DYSENTERY

WITH NOTES ON MESENTERIC ADENITIS AND INFLAMMATION OF THE DISTAL PORTION OF THE ILEUM

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The importance of recognizing a form of bacillary dysentery the symptoms of which are mistaken for those of acute appendicitis has been suggested in two general studies [1] of recent outbreaks of Sonne-Duval and atypical Flexner dysentery. The purpose of the present report is to point out the clinical, bacteriologic, serologic and pathologic features distinguishing bacillary dysentery from acute appendicitis.

The group studied in the one year period between December 1933 and December 1934 included approximately 300 cases of Sonne-Duval and atypical Flexner bacillary dysentery. These cases occurred chiefly within the metropolitan area (New York City, Jersey City and their environs). Some occurred on three transatlantic liners, the disease having apparently started on board ship. The incidence and widespread nature of bacillary dysentery can perhaps be surmised from the observation made by my associates and me that many cases are unrecognized by the physician because of the mild and transitory symptomatology or because the patients do not seek medical attention. There are also certain factors in the bacteriologic and serologic aspects of the disease which militate against accurate diagnosis by any but the most painstaking technic and perseverance. And, finally, the general opinion of the prevalence of bacillary dysentery in the summer season does not seem to apply to Sonne-Duval dysentery. For the outbreak which we reported on, like others, occurred during the winter. Environmental and hygienic factors largely govern the incidence of the disease, which is endemic the year round. With these basic facts in mind I shall attempt to point out the essential clinical features of one form of bacillary dysentery—the appendicular type.

The frequency of the appendicular form of bacillary dysentery was approximately 3 per cent in both the Sonne-Duval and the atypical Flexner type of the disease. Most of the cases in this series have been in children, although there was a high general incidence of dysentery in adults.

From the Department of Laboratories and Research of the Bronx Hospital.

1. Felsen, J., and Osofsky, A. G.: Sonne Dysentery, J. A. M. A. **103**:966 (Sept. 29) 1934. Felsen, J.; Rundlett, E. V.; Sullivan, J., and Gorenberg, H.: Atypical Flexner Dysentery: A Preliminary Report of the Jersey City Epidemic, ibid. **103**:1055 (Oct. 6) 1934.

CLINICAL ASPECTS

The usual clinical features of the appendicular type of bacillary dysentery are colicky abdominal pain, often localized to the right lower quadrant, vomiting and only moderate pyrexia, with a temperature of from 101 to 102 F. There may be lassitude, anorexia and headache in the prodromal period, but these symptoms are less likely to occur in the Sonne-Duval than in the Flexner type of dysentery. Tenderness

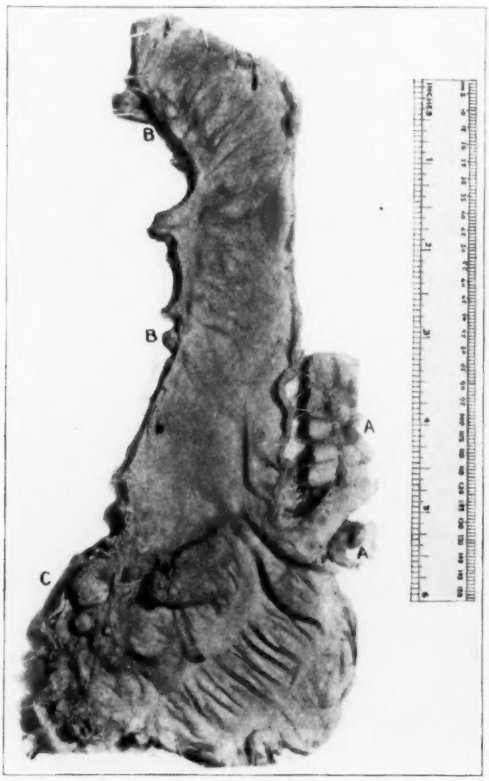

Fig. 1.—Intestine in a case of Flexner dysentery. The enlarged mesenteric nodes along the margin of the appendix at *A* and the ileum at *B* and the large nodes on the cecum at *C* are apparent.

is generally present at or about McBurney's point; it may be most manifest on rebound and may shift with change in the position of the body. The ileum and colon are generally spastic, and in thin children the ileum and sigmoid flexure may actually be felt through the abdominal wall. This point is an important clinical diagnostic feature, because intestinal spasm occurs early in the disease and persists for some time. In routine examination a spastic ileum or sigmoid flexure

felt through a lax abdominal wall should immediately suggest bacillary dysentery. In young children enlarged mesenteric nodes can often be felt at the ileocecal angle. A history of diarrhea is helpful in reaching a diagnosis, particularly if mucus and bright red blood have been present. The latter feature, however, may not be evident or else may be noted only as red specks sprinkled on soft fecal material. Profuse watery, foul, greenish stools are often encountered. However, in some

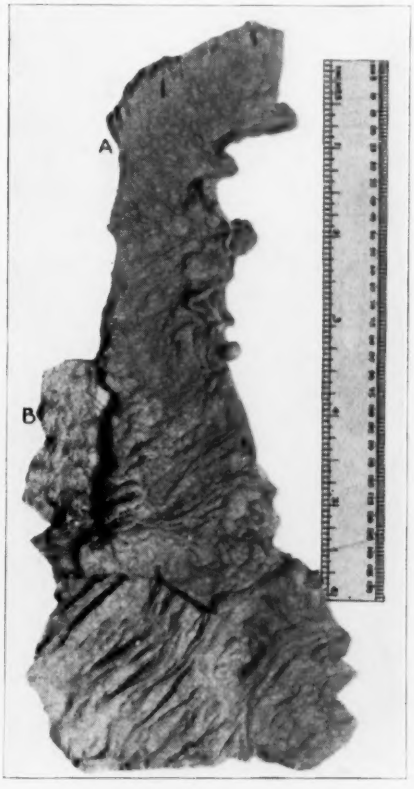

Fig. 2.—Mucosal aspect of the specimen the external appearance of which is shown in figure 1. Follicular lymphoid hyperplasia is seen as multiple small punctate elevated areas (*A*). These areas are also present in the appendix (*B*) and may account for the symptoms referable to this organ.

of our patients no diarrhea occurred, and in almost one-half obstinate constipation followed subsidence of acute symptoms after from the sixth to the tenth day. This must be borne in mind, as often appendicular symptoms ("appendicism") may occur in cases of bacillary dysentery on or after the sixth day, when diarrhea is no longer a prominent feature. The leukocyte count in the early stage of bacillary dysentery is likely to

be normal, or there may be actual leukopenia. The latter finding was a notable feature in most of our cases of the appendicular type of both Sonne-Duval and Flexner dysentery. Clayton [2] and Nelson [3] reported cases in which the Sonne-Duval type of dysentery was mistaken for appendicitis. When the diagnosis of bacillary dysentery has been overlooked the patient is promptly operated on, and the usual observations

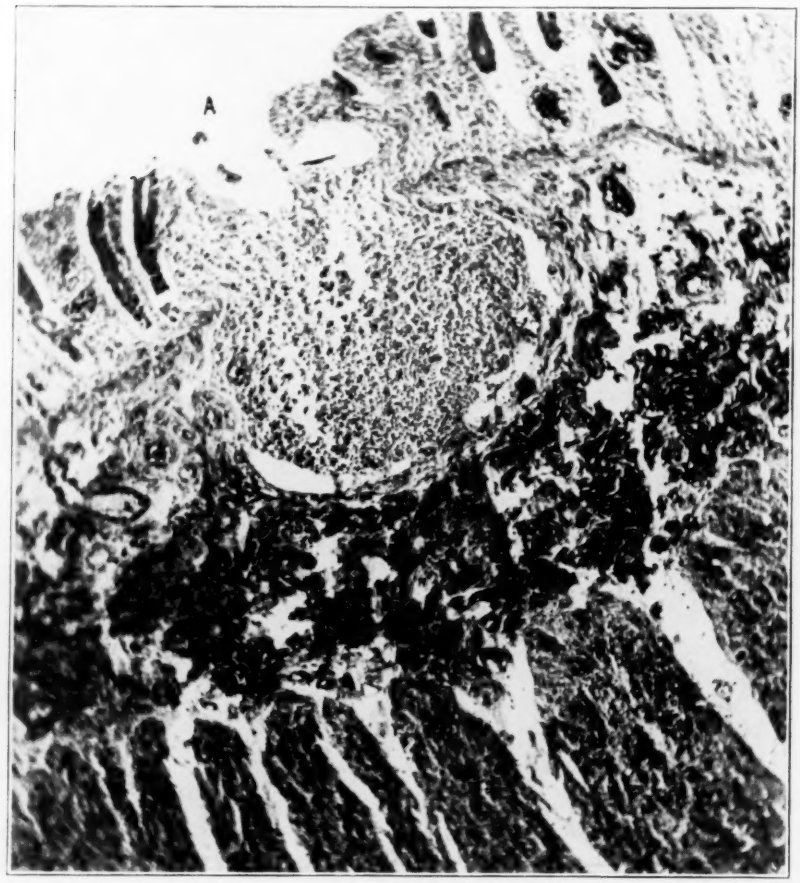

Fig. 3.—Microscopic appearance of an acuminate solitary lymph nodule with ulceration of the overlying mucosa (*A*) in a case of Sonne-Duval dysentery.

are a normal-appearing appendix but a rather mystifying mesenteric lymphadenitis which may be localized to the ileocecal region or to the

2. Clayton, F. H. A.: A Case of Sonne Dysentery in England, Lancet **1**:39, 1927.

3. Nelson, R. L.: Sonne Dysentery: A Report of Thirty Cases of Dysentery in Children Caused by B. Dysenteriae Sonne, Am. J. Dis. Child. **41**:15 (Jan.) 1931.

mesenteric border of the ileum. In some cases the entire mesentery is studded with enlarged, pinkish to reddened nodes as far as the attachment to the posterior abdominal wall. These nodes vary from a few millimeters to 2 or 3 cm., those of the latter size generally being encountered at or near the ileocecal angle. In 4 cases [3a] of our series in which the patient was operated on there was also acute inflammation of the terminal portion of the ileum. In 2 of these (cases 5 and 7) the organism was of the Flexner type, both the patients being adults. Two cases (2 and 4) were of the Sonne-Duval type and occurred in children. In all 4 cases and in 1 other (case 1) mesenteric adenitis was present. It might perhaps be of interest to note that the postoperative cases were studied because we learned of the observation of mesenteric lymphadenitis, with or without inflammation of the terminal (distal) portion of the ileum, through the interest of surgeons who were acquainted with recent investigations in this field. Communications from other sources indicate the fairly high frequency of the finding of this condition in routine appendectomies without any satisfactory local pathologic condition to explain the lymphadenitis. The following cases are typical, illustrating many of the clinical features already noted.

REPORTS OF CASES

CASE 1.—M. S., a girl aged 8 years, in the service of Dr. W. Klein, to whom the disease in the outbreak of Sonne-Duval dysentery occurring in New York City was finally traced, had been discharged eight weeks previous to the time of investigation. On admission to the Bronx Hospital the patient complained of pain in the right loin, radiating to the umbilicus, of one day's duration. There were anorexia, headache and several attacks of vomiting. Physical examination revealed tenderness in the loin and over McBurney's point. The urine contained albumin. The total leukocyte count was 4,000 cells per cubic millimeter. The temperature at the time of admission was 101.2 F. At operation the appendix was observed to be normal, but there was mesenteric lymphadenitis at the ileocecal angle. Sections revealed moderate lymphoid hyperplasia of the solitary nodules of the intestine and marked lymphoid hyperplasia in the excised node without necrosis. On the day of admission there were many diarrheal bowel movements, the exact number of which was not recorded. Subsequently, the average daily number was seven, bright red blood being present during the first three days. The postoperative temperature varied from 98.6 to 100 F. The patient at no time appeared seriously ill. On the day of discharge there were eight loose stools. We learned of this case only in the course of our epidemiologic survey, eight weeks after the patient's discharge. We succeeded, however, in obtaining specimens of the blood and feces which gave positive results in tests for Bacillus dysenteriae Sonne-Duval ten weeks after operation. The positive cultures obtained from fecal material and the high agglutination titers continued to be present for approximately four months, although the child appeared to be well.

3a. Since this paper went to press 8 additional cases of acute inflammation of the distal portion of the ileum associated with bacillary dysentery have been studied.

Case 2.—R. G., a boy 7 years of age, in the service of Dr. S. Cohn, was admitted to the hospital on Nov. 21, 1934, complaining of a cramplike pain in the umbilical region of three days' duration. The onset was sudden, unaccompanied by vomiting or other symptoms and persisted until the time of admission. Physical examination revealed tenderness at McBurney's point. The total leukocyte count was 10,100 cells per cubic millimeter with 63 per cent mature polymorphonuclear neutrophils, 6 per cent band forms, 23 per cent small lymphocytes and 8 per cent monocytes. The urine contained 1.3 per cent sugar and a trace of acetone. The patient was operated on approximately two hours after admission. A large amount of free serous fluid was noted in the right lower quadrant of the abdomen and in the pelvis. The cecum was undescended, and there were numerous large mesenteric lymph nodes near the cecum and ileum and in the mesenteriolum of the appendix. These varied from 4 to 15 mm. in their largest diameters. The largest one was situated on the cecum. The terminal 3.5 cm. of the ileum was markedly thickened. Pathologic examination revealed an appendix 8 cm. in length with evidence of periappendical adhesions. The serosal surface was smooth, and the mucosa was hyperplastic and showed areas of focal necrosis. A lymph node accompanying the appendix was 2.5 by 1.5 cm. Microscopic section revealed hyperplasia of the solitary lymph nodules with periappendical edema. Section of the lymph node showed acute lymphadenitis. The temperature on admission was 100 F., with a temporary postoperative increase to 101.4 F. This elevation occurred on the day after operation, and thereafter the temperature varied slightly around 99 F. There were no bowel movements during the entire stay in the hospital except after an enema; the patient was discharged as well eleven days after admission. Cultures of the feces on November 24 and November 30 were negative for the typhoid-dysentery group, but on November 24 the blood showed an agglutination titer for B. dysenteriae Sonne-Duval of 1:100, which fell in six days, two days before the patient's discharge, to 1:40. The diagnosis was dysentery of the Sonne-Duval type with inflammation of the distal portion of the ileum and mesenteric adenitis.

Case 3.—F. R., a boy 8 years of age (in the service of Dr. H. Heiman), was admitted to the hospital on Dec. 11, 1934, with complaints of abdominal pain and fever for one week and bloody stools for two weeks. The pain was localized in the umbilical region, and its onset was accompanied by vomiting. On the day of admission the patient had five bloody stools. Physical examination revealed a pale, undernourished, thin boy, who appeared to be only moderately ill. The abdomen was scaphoid and soft, but there was tenderness in the left upper quadrant. There was a positive Murphy sign. A history obtained subsequently from the mother elicited the information that prior to the onset of the child's illness the bowels had been constipated and that she had noted a great deal of mucus and blood in the stools for approximately one week prior to his admission. The temperature on his admission was 101 F.; it fell rapidly to the normal level on the next day and continued so until the patient's discharge from the hospital eighteen days after admission. Except on the first day of hospitalization, when eight bloody stools were noted, only one or two stools were recorded a day. This child appears to have been admitted at the end of his illness and had a rapid convalescence. On December 11 B. dysenteriae Sonne-Duval was isolated from the feces, but no agglutination was present. On December 13 again no agglutination was present. On December 18 the blood showed an agglutination titer for B. dysenteriae Sonne-Duval of 1:160, and the organism was recovered again from the feces. A third positive culture was obtained on December 27. Diagnostic

bacteriophage was found in the last two examinations. The diagnosis was dysentery of the Sonne-Duval type with suggestive appendicular symptoms.

CASE 4.—J. A., a girl 5 years of age (in the service of Dr. S. Cohn), was admitted to the hospital on Dec. 18, 1934, with a history of pain in the right lower quadrant for two days. The pain was intermittent and was situated near the umbilicus. Anorexia was present. The abdomen was soft and obese, and tenderness was present at McBurney's point. There was no tenderness on rebound, and no mass was felt. The leukocyte count on the day of admission was 6,800 cells per cubic millimeter with 63 per cent mature polymorphonuclear neutrophils, 2 per cent band forms, 27 per cent small lymphocytes and 8 per cent monocytes. The urine contained acetone and diacetic acid. Appendectomy was performed shortly after admission. The appendix appeared normal. The terminal 3.5 cm. of the ileum was thickened. There were numerous small lymph nodes, approximately 4 mm. each, in the mesentery of the terminal portion of the ileum, and one large node, approximately 2 cm., was located on the posterior surface of the cecum at the ileocecal junction. Pathologic examination revealed an appendix 5 cm. long with no essential pathologic feature other than periappendical adhesions. The temperature on admission was 100.4 F., and it ranged about that level until the patient's discharge on the twelfth day of hospitalization. There were no bowel movements, except on the first day, when two occurred. None of the stools were bloody. On December 20 the agglutination titer for B. dysenteriae Sonne-Duval was 1:40, but the culture of the feces was negative. On December 26 the blood showed an agglutination titer of 1:200 for B. dysenteriae Sonne-Duval and diagnostic bacteriophage for the same organism. The culture of the feces was negative. The diagnosis was dysentery of the Sonne-Duval type with inflammation of the distal portion of the ileum and mesenteric adenitis.

CASE 5.—B. S., a girl 19 years of age (in the service of Dr. W. Klein), was admitted to the hospital on Oct. 5, 1934, with a history of having had "indigestion" accompanied by flatulence after the ingestion of food for ten days. Until two days prior to admission there was generalized abdominal pain, which subsequently localized in the right lower quadrant. No diarrhea was present. Physical examination revealed tenderness in the right lower quadrant just below, and to the right of, the umbilicus. There was no rigidity. The patient appeared to be well. Appendectomy was performed on October 6. The distal 45 cm. of the ileum was red, hyperemic, swollen and thickened. The mesenteric lymph nodes appeared to be inflamed and were greatly enlarged. The appendix was normal, measuring 5 cm. in length, and microscopic section revealed only lymphoid hyperplasia. The temperature throughout the eleven days in the hospital varied between 99 and 100 F., and bowel movements were obtained only by the use of enemas. Cultures of the feces on October 16 and October 19 were negative for B. dysenteriae, but on October 9 and 16 positive agglutination titers of 1:100 for Bacillus dysenteriae Flexner were obtained. The diagnosis was bacillary dysentery of the Flexner type, with inflammation of the distal portion of the ileum and mesenteric adenitis.

CASE 6.—S. F., a girl 15 years of age (in the service of Dr. S. Cohn), was admitted to the hospital on Dec. 23, 1934, with a history of intermittent pain in the right lower quadrant for the past three weeks. One brother, aged 21, had been under treatment for ulcerative colitis for the past year, and I have since examined another brother. Physical examination revealed slight tenderness in the right lower quadrant. The leukocyte count on the day after admission was 12,300 cells per cubic millimeter with 69 per cent mature poly-

morphonuclear neutrophils, 3 per cent band forms, 22 per cent small lymphocytes, 5 per cent monocytes and 1 per cent basophils. On December 24 appendectomy was performed, but the appendix appeared to be normal, except for periappendical adhesions. It was 6 cm. in length, and section showed subserosal edema. The temperature varied between 99 and 100 F. during the first two days of hospitalization with a temporary postoperative increase to 102.4 F. There were fourteen loose stools on the second day after operation and sixteen bowel movements in the next three days. Culture of the feces on December 26 showed B. dysenteriae Flexner, and the agglutination titer for this organism on the same day was 1: 100. The diagnosis was bacillary dysentery of the Flexner type with appendicular symptoms.

CASE 7.—F. F., a woman aged 20 (in the service of Dr. W. Klein), was admitted to the hospital on Aug. 11, 1934, with a history of illness following the ingestion of frankfurters eight days before. The patient suffered from constipation until three days prior to admission, when diarrhea occurred and was accompanied by vomiting. Physical examination revealed tenderness in both the left and the right lower quadrant with shifting tenderness when the patient was turned from side to side. On August 12 the leukocyte count was 8,300 cells per cubic millimeter with 41 per cent mature polymorphonuclear neutrophils, 21 per cent band forms, 27 per cent small lymphocytes and 11 per cent monocytes. The patient underwent operation on August 13. The terminal 30 cm. of the ileum was engorged, and the wall markedly thickened. This area ended abruptly at its upper limit where there was a definite line of demarcation from the normal intestine. There were many enlarged mesenteric nodes, which appeared to be acutely inflamed. The appendix was 6 cm. in length and appeared normal. On section there was no evidence of acute inflammation. The temperature on admission was 101.6 F., and it varied little from this level until the tenth day of hospitalization, when it fell to normal. The patient was discharged on August 23. During the entire period there had been no bowel movements, except on three occasions when enemas were administered. Cultures of fecal material revealed the presence of B. dysenteriae Flexner, and the blood showed an agglutination titer of 1: 100 for the same organism. The diagnosis was bacillary dysentery of the Flexner type, with inflammation of the distal portion of the ileum and mesenteric adenitis.

PATHOLOGY

All the postmortem specimens obtained in our cases of atypical Flexner and of Sonne-Duval dysentery exhibited marked mesenteric adenitis, which is part of the picture of generalized lymphoid hyperplasia involving the solitary nodules of the intestinal tract, Peyer's patches and the mesocolic nodes. The mucosa of the appendix, colon and terminal part of the ileum is studded with punctate elevated areas, the size of a pinhead, which stand out prominently on a reddened background. The mucous membrane may exhibit superficial ulcerations, or they may be entirely absent. In the cases of milder and moderately severe infection there appears to be capillary oozing through relatively intact epithelium. The mucosa seems to weep blood. Patches of adherent grayish membrane may be present, together with mucus, pus and bright red blood. The enlarged nodes at the ileocecal angle, extending to the anterior and posterior aspects of the cecum, stand out promi-

nently. Chains of nodes also extend upward along the mesenteric border of the ileum. The cecal nodes are sometimes as large as a hazelnut. It is in the terminal portion of the ileum and in the cecum that the most advanced pathologic changes are often noted. After fixation in formaldehyde there is dimpling of the central portions of the enlarged solitary lymph nodules due to central necrosis with softening.

Microscopic sections reveal generalized lymphoid hyperplasia, and often the epithelium overlying the acuminate lymph nodules is necrotic, so that the lymphoid tissue appears to project into the lumen of the bowel. It is our opinion that these changes are toxic effects, as are those in the spleen. The changes in the latter organ consist essentially of hemorrhagic halos outlining the lymph nodules and congestion and edema of the splenic pulp. The halos are striking and are made up largely of macrophages loaded with blood pigment. Positive cultures may occasionally be obtained from the mesenteric nodes. We have repeatedly reproduced the disease in rabbits by intravenous injection of the organism, after which the bacteria have been recovered from the feces. This suggests, as Flexner had previously pointed out, that the intestinal lesions are due to toxic effects during the process of excretion from the blood vessels through the intestinal wall into the lumen.

BACTERIOLOGIC DIAGNOSIS

Our experience in the recent outbreaks has been that the Sonne-Duval and atypical Flexner organisms have a transitory existence in the intestinal canal. Most of the positive cultures in our studies have been obtained in the first week of the disease, during the acute stage when profuse diarrhea with blood and mucus is present. The organism, however, has also been recovered in the period of convalescence and even from patients suffering from constipation. The best procedure is to make cultures daily for ten days before discontinuing the search. In some cases cultures fail to reveal the organism even after the most painstaking investigation, although the agglutination tests show a steady increase in the titer of the serum. Some of these patients, however, show a positive diagnostic bacteriophage which appears to be group-specific rather than type-specific. In this test, as in the studies on agglutination, eighteen-hour cultures of the Shiga, Mount Desert, Park-Hiss, Flexner and Sonne-Duval organisms are used, and of the last two forms, several recently isolated strains. The diagnostic bacteriophage obtained from the fecal filtrate appears to be almost as transitory as the dysentery organism in the feces and the agglutination titer, particularly in the cases of the Sonne-Duval type. The highest agglutination titer has been obtained in the serum during the second or third week in the Sonne-Duval type of dysentery and somewhat later in the atypical

Flexner type. Ordinarily, fresh fecal specimens may be used for bacteriologic study, but in some cases gentle scraping of the colonic mucosa with a small dull curet or a stiff wire loop may be required.

While Ritchie's studies of 792 normal serums suggest the wide prevalence of high agglutination titers for B. dysenteriae and, therefore, of the disease itself, we have been unable to verify this with regard to Sonne-Duval dysentery in our control studies of 300 serums obtained from persons in the city of New York. It may be that in regions where dysentery is prevalent such serologic findings are common. We are convinced, however, of the increasing frequency of both the Sonne-Duval and the Flexner type on the eastern seaboard, and also that the disease in this region is overlooked with surprising frequency. During August 1934 we studied cases of Flexner dysentery occurring in groups on three transatlantic liners, apparently commencing on board ship and involving physicians on two of them. While we were unable to study the cases of all the persons having the disease, we were assured of the wide prevalence of similar dysenteric symptoms in many other instances. We have encountered many cases in the city of New York, and suggestive outbreaks have occurred in some of the hospitals. The strange feature is that, because of the transitory character of the disease in the mild form, cultures are not made; agglutination studies are not carried out, and the diagnosis is overlooked. For this reason also the department of health is generally unaware of any widespread occurrence of bacillary dysentery.

DIAGNOSIS

In a case in which the condition is suspected to be acute appendicitis it is manifestly unwise to wait for the results of culture. In children particularly a history of colitis or acute diarrhea, with or without mucus and blood, is suggestive of dysentery. It is always well to inquire whether other children or adults in the family or playmates have had recent diarrhea. The incubation period being a matter of only from twelve hours to two days, the information obtained is generally reliable. Examination reveals a soft abdomen or questionable rigidity, though pain and tenderness may be definite. Intestinal spasm, particularly involving the terminal portion of the ileum or sigmoid flexure, may be felt if the abdominal wall is sufficiently thin or relaxed. Examination with the patient in a warm bath facilitates palpation of the enlarged lymph nodes and the spastic intestine. The patient often appears well and comfortable, out of all proportion to the severity of the bloody stools. There is only moderate initial pyrexia (temperature from 100 to 101 F.), and the blood shows a normal leukocyte count or actual leukopenia early in the disease. When a short delay entails no undue risk the true nature of the disease is soon manifest, the symptoms referable to the appendix subsiding while the diarrhea per-

sists, usually to a greater degree. By this time studies of cultures, agglutination titers and bacteriophage establish the diagnosis with certainty. When fresh cultures are at hand preliminary studies on agglutination may be completed in a few hours, cultures of the feces in eighteen hours and tests for diagnostic bacteriophage in from five to seven hours.

The following tabulation shows the points to be considered in the differential diagnosis.

DIFFERENTIAL DIAGNOSIS

Appendicular Form of Bacillary Dysentery	*Acute Suppurative Appendicitis*
1. History of "food poisoning"	1. Sudden onset, often without history of dietary indiscretion
2. History of diarrhea or contact with a person who has had diarrhea	2. Diarrhea unusual; no history of contact
3. Moderate initial pyrexia	3. Higher initial pyrexia
4. Lax abdominal wall	4. Muscular rigidity
5. Spastic ileum or sigmoid flexure	5. No spasm of ileum or sigmoid flexure
6. Enlarged mesenteric nodes felt at the ileocecal angle in thin children	6. Mesenteric nodes usually not felt
7. Patient appearing well and relatively comfortable	7. Patient acutely ill
8. Absence of leukocytosis; leukopenia frequent	8. Leukocytosis with increase in band forms
9. Positive culture obtained from the feces early in the disease	9. Culture obtained from the feces negative for B. dysenteriae
10. Agglutination titer present late in the disease	10. No agglutination of B. dysenteriae except in some patients who have recently recovered from the disease
11. Diagnostic bacteriophage present	11. No diagnostic bacteriophage, except as noted in circumstances specified in item 10
12. Appendix grossly appearing normal	12. Appendix acutely inflamed
13. Mesenteric adenitis	13. Mesenteric adenitis rarely as pronounced as in bacillary dysentery
14. Appendicular lymphoid hyperplasia with focal necroses of the solitary lymph nodules	14. Appendicular necrosis with suppuration or gangrene
15. Inflammation of the distal portion of the ileum in some cases	15. No inflammation of the distal portion of the ileum
16. Hyperplasia of Peyer's patches and solitary acuminate lymph nodules in the appendix, ileum and colon	16. Ileum and colon not involved; intramural acute suppurative inflammation of all the coats of the appendix
17. Appendicular symptoms usually clear until within twenty-four hours or less, but persisting diarrhea of increasing severity	17. Appendicular symptoms persisting
18. Removal of appendix unnecessary	18. Removal of appendix imperative

SUMMARY

Attention is called to a type of bacillary dysentery characterized by the presence of mesenteric adenitis, with or without inflammation of the terminal portion of the ileum. The symptomatology closely simulates that of acute appendicitis. The general clinical and diagnostic features are described.

Case Reports

ERYTHROBLASTOSIS IN THE NEW-BORN

REPORT OF FOUR CASES

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AND
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Edema of the new-born was described as far back as the seventeenth century. In 1892 Ballantyne [1] presented an excellent dissertation on this disease, and reviewed the literature, from which he collected about sixty cases. Edema with disturbance of the hematopoietic organs was first noticed by Schriddle [2] in 1910; since then many reports have been published, most of which are in the German literature.

A case probably of icterus gravis was reported in 1873, but the credit for describing the disease as being familial belongs to Pfannenstiel,[3] who in 1908 reported two fatal cases and reviewed the literature. Buchan and Comrie [4] reported the morbid anatomy in five cases found in two families. This report was the first in which nucleated red cells were described.

Rautman [5] first used the term erythroblastosis to describe the underlying condition found in general edema of the fetus. I. A. Abt [6] was the first American author to discuss familial icterus.

In this country Buhrman and Sanford [7] described the abnormal red cells and gave a complete report of two cases. In the same year (1931)

From the Departments of Pediatrics and Pathology, School of Medicine, University of Louisville.

1. Ballantyne, J. W.: Diseases of the Foetus, Edinburgh, Oliver & Boyd, 1898.
2. Schriddle, H.: München. med. Wchnschr. **57**:392, 1910; Deutsche. med. Wchnschr. **37**:432, 1911.
3. Pfannenstiel, J.: München. med. Wchnschr. **55**:2169, 1908.
4. Buchan, A. H., and Comrie, J. D.: J. Path. & Bact. **13**:398, 1909.
5. Rautman, H.: Beitr. z. path. Anat. u. z. Allg. Path. **54**:332, 1912.
6. Abt, I. A.: Familial Icterus of New-Born Infants, Am. J. Dis. Child. **13**:231 (March) 1917.
7. Buhrman, W. L., and Sanford, H. H.: Is Familial Jaundice of New-Born Infants Erythroblastosis? Am. J. Dis. Child. **41**:225 (Feb.) 1931.

Ferguson[8] described the histopathologic changes in six cases of erythroblastosis with jaundice and edema of the new-born.

The next year Clifford and Hertig[9] reported seven cases and discussed the clinical picture of the disease. In the same year Diamond, Blackfan and Baty[10] made an excellent report on erythroblastosis foetalis and reviewed the literature. They reported twenty cases (two of general edema, twelve of icterus gravis neonatorum and six of anemia of the new-born).

In 1933 the American authors were Abt,[11] who reported two cases and offered a substitute name—"embryonal hematopoietic persistence"—for erythroblastosis, and Warstrum,[12] who described the condition of "erythroleukoblastosis."

We are adding to this list the report of four cases with postmortem observations in one.

REPORT OF CASES

CASE 1.—Baby J., a white girl, was admitted to the ward after delivery on Aug. 4, 1932. The mother, a primipara, came to delivery after about eight months of a normal pregnancy. The Wassermann reaction of the blood was negative. The second pregnancy, which occurred one year later, was normal, but resuscitation was difficult. At present this child is entirely normal.

On the day following delivery the patient was jaundiced and had a generalized petechial eruption that was more pronounced over the upper part of the trunk and face. At this time the liver was palpable and the spleen was enlarged to about 2.5 cm. below the costal margin. Analysis of the blood revealed: red cells, 5,490,000; white cells, 9,250, with 42 per cent neutrophilic leukocytes, 53 per cent lymphocytes, 2 per cent eosinophils and 3 per cent myelocytes; hemoglobin content, 78 per cent (Sahli); platelets, 270,000; many normoblasts, and clotting and bleeding time prolonged. A transfusion of 50 cc. of citrated blood was given through the fontanel.

The next day the infant was more jaundiced and did not appear to be improved, so 50 cc. of citrated blood as again given. The following day 40 cc. of citrated blood was administered intramuscularly. The clotting time was four minutes, and the bleeding time, three and one-half minutes.

On August 15, eleven days after birth, a blood test showed: 4,120,000 red cells, 13,400 white cells, with 54 per cent neutrophilic leukocytes, 42 per cent lymphocytes, 1 per cent myelocytes, 1 per cent eosinophils and 2 per cent unidentified cells, and hemoglobin content, 120 per cent. There were fewer normoblasts, but the actual count was not reported.

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8. Ferguson, J. A.: Am. J. Path. **7**:277, 1931.
9. Clifford, S. H., and Hertig, A.: New England J. Med. **207**:105, 1932.
10. Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: J. Pediat. **1**:269, 1932.
11. Abt, A. F.: J. Pediat. **3**:7, 1933.
12. Warstrum, A. C.: Am. J. Path. **9**:623, 1933.

On August 16 the icterus index was 200; the direct van den Bergh test gave an immediate reaction. Roentgenograms of the bones gave no evidence of syphilis; the Wassermann reaction was negative. There were a few clay-colored stools. The baby died on August 16, the twelfth day after birth. Postmortem examination was not permitted.

CASE 2.—Baby C., a Negro girl, was admitted to the ward following delivery on June 21, 1933. The mother, a primipara, came to delivery after a normal period of gestation. The Wassermann reaction was negative.

On admission to the ward the child was jaundiced. Blood taken for examination revealed: 3,650,000 red cells; 12,400 white cells, with 65 per cent neutrophilic leukocytes, 16 per cent lymphocytes, 19 per cent myelocytes and nucleated red

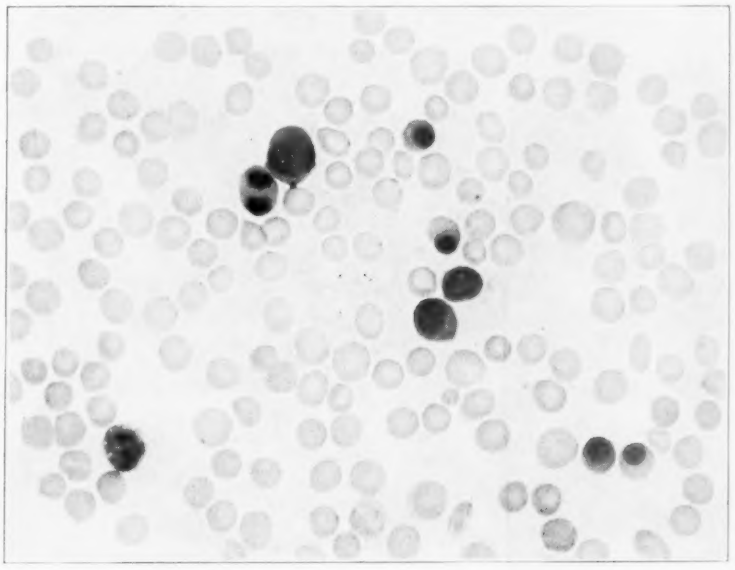

Fig. 1 (case 2).—A blood smear, showing many nucleated red cells and one cell in mitosis.

cells, 34 per cent of the total number of the nucleated cells (fig. 1); icterus index, 43, and clotting and bleeding time, prolonged.

The next day petechial and ecchymotic spots were noted over the body. A transfusion of blood was started, but during the course of the transfusion the baby began to gasp for breath, vomited blood and died of what was thought to be a pulmonary hemorrhage.

Postmortem Examination revealed jaundice of the skin, sclera and mucous membranes. Petechiae from 1.5 to 2 mm. in diameter were diffusely scattered over the entire body, and in the palpebral conjunctivae were a few similar lesions. In the scrotum was an ecchymosis 4 cm. in diameter, and in the skin of the limbs and trunk were a few smaller but similar hemorrhages. Partially clotted blood was in the anterior portions of the nares and the mouth. There was no excess fluid in the body cavities.

The cardiac muscle was light and soft. Sections showed marked hydrops.

The lungs were crepitant throughout. In the pleura and scattered throughout were many petechiae. Bloody frothy fluid could be expressed from the bronchi. Sections revealed small, recent hemorrhages into the air sacs, bronchioles and bronchi. No blood was seen in the mucosa of the bronchioles, but was seen in the alveolar septums. It is probable, therefore, that the hemorrhage was the result of capillary oozing into the alveolar sacs, from which the blood flowed through the alveolar ducts to the bronchial tree. A number of lobules of lung tissue were partly atelectatic, evidently from occlusion of bronchi by blood.

Occasionally giant cells were seen among the cells lining the alveolar sacs; a few were detached and free in the lumen (fig. 2). Those attached were in position on the basement membrane and seemed to be derived from the epithelium. They were identical with those in the skin and kidney.

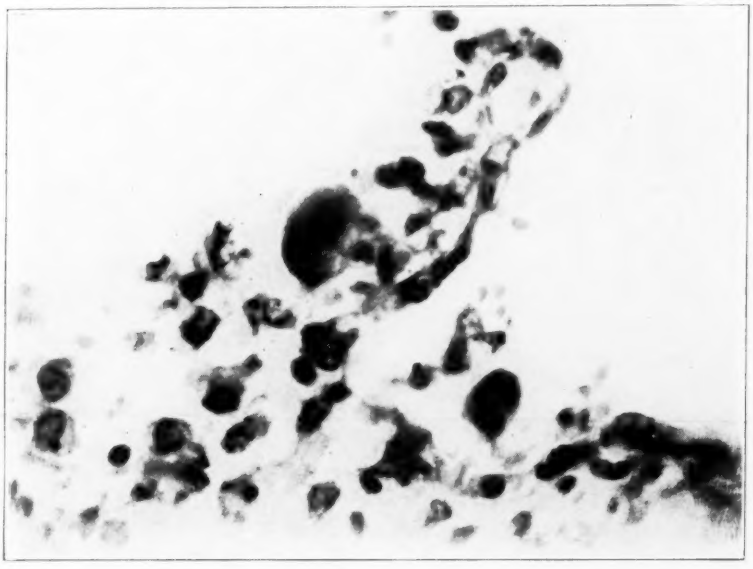

Fig. 2 (case 2).—A section of lung, showing a large atypical epithelial cell attached to the wall of the alveolus and protruding into the lumen.

There were no gross changes in the thymus gland.

The liver was not enlarged. It was deeply jaundiced, as were all the tissues. No obstruction of the bile passages was demonstrated. The gallbladder contained about 15 cc. of very dark bile. Sections showed most of the liver cells to be faintly stained and markedly vacuolated. A few cells consisted of a membrane-like outer portion with a reticulated cytoplasm which seemed to suspend the nucleus. Most cells were densely pigmented with hemosiderin, and a few contained bile. Occasional canaliculi were distended with bile pigment in small localized areas only. There was definite evidence of mechanical obstruction, but it was not demonstrated. Since the distended bile canaliculi were so few and since there was marked damage to the liver cells, many of them being densely stained with bile pigment, it seems probable that mechanical obstruction was not the sole cause of the jaundice, but that there was also a suppression of function of the liver cells. A few of the bile ducts were distended, but most of them were collapsed.

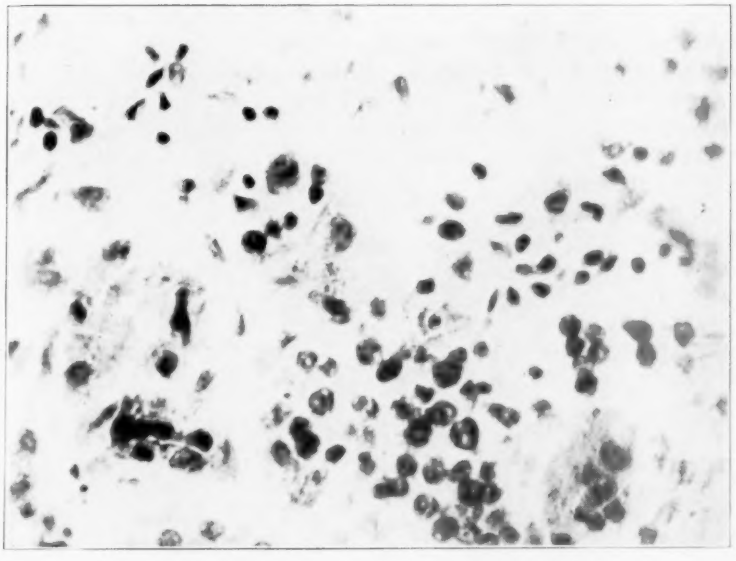

Fig. 3 (case 2).—A section of the liver showing one canaliculus distended with bile, bile pigment in the liver cells and one hematopoietic center in a lobule of hepatic tissue.

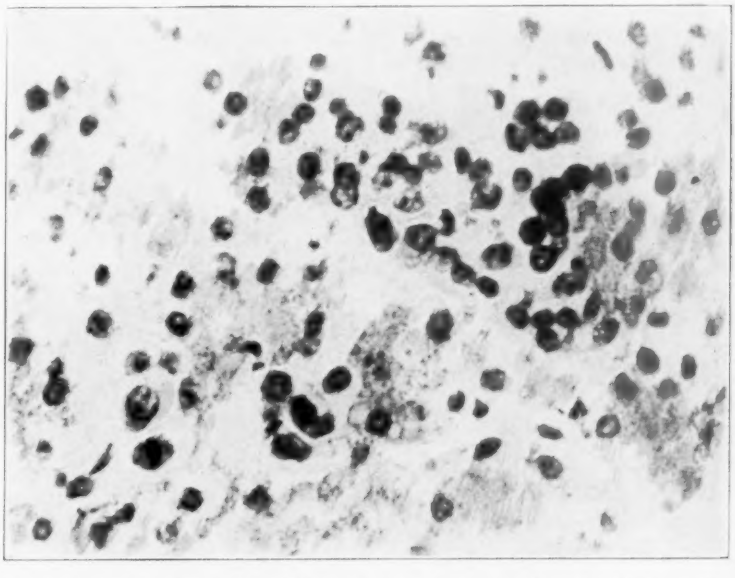

Fig. 4 (case 2).—A section of the liver showing one hematopoietic center and the large liver cells laden with old blood pigment.

Scattered throughout the liver substance with no special reference to septums or lobules were hematopoietic centers. These were small but so numerous that eight or ten could be seen in one low power field. There was no demonstrable relationship between them and the obstructed bile ducts. There was no pressure atrophy about them. These centers were composed of both red and white cells. Many of the red cells were nucleated and a moderate number were in mitosis. A few of the white cells were definitely polymorphonuclears, others appeared to be more primitive forms of the same cells and many could not be definitely classified. None of them were considered to be lymphocytes (figs. 3 and 4).

The spleen was enlarged and tense. Sections showed an occasional small hematopoietic center in the connective tissue about the vessels or in the walls of the blood sinuses, but none in the lymph follicles (fig. 5).

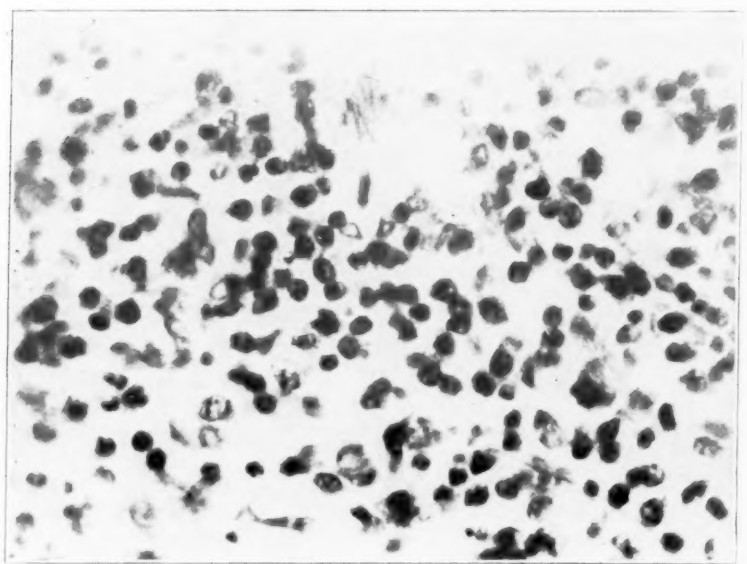

Fig. 5 (case 2).—A section of the spleen, showing a large hematopoietic center in the walls of the blood sinuses.

Sections of the pancreas showed few blood-forming centers in the connective tissue, especially near large blood vessels.

The kidneys were markedly lobulated. The sections revealed a few large hematopoietic centers in the cortex. A number of convoluted tubules were partly or completely lined with large cells identical with those in the lung and skin. In some instances these cells were in juxtaposition to normal-appearing epithelial cells. They were polygonal and twice the normal size. The cytoplasm was finely granular and in some instances vacuolated (degeneration). The nucleus was round or oval and had a dense outer membrane and a large, very dense oval or round central portion. These atypical cells are not accounted for (figs. 6 and 7).

The adrenal glands were not remarkable.

The gastro-intestinal tract contained bloody material. There were no ulcerations, the hemorrhage apparently being due to terminal capillary oozing.

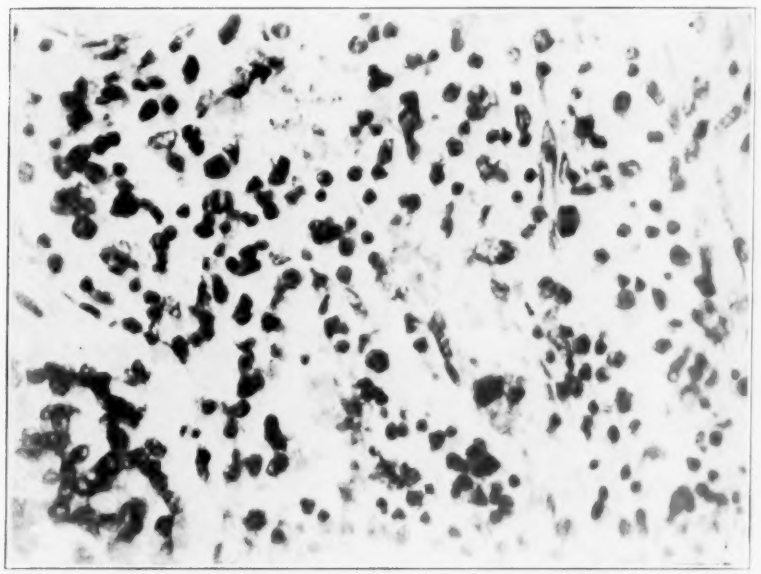

Fig. 6 (case 2).—A section of the kidney showing one hematopoietic center in the cortex.

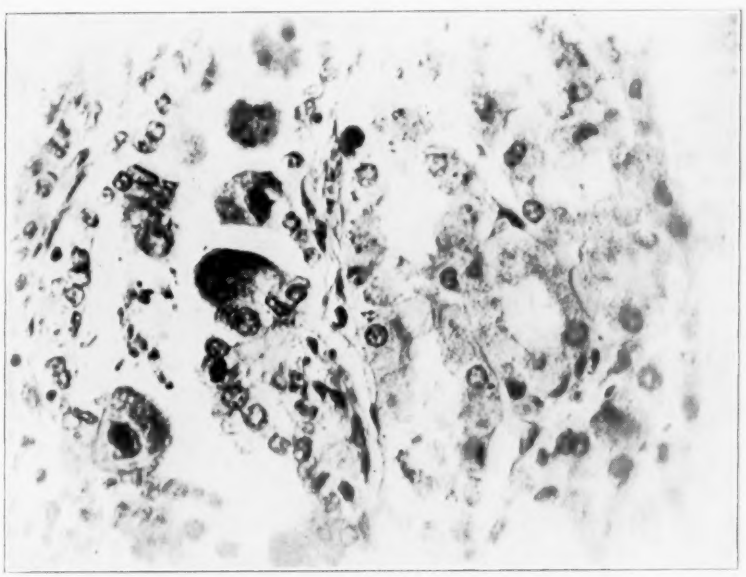

Fig. 7 (case 2).—A section of the kidney showing a convoluted tubule lined by large atypical cells which are continuous with the normal epithelium.

The lymph nodes were not remarkable macroscopically, and sections revealed no blood-forming centers. Sections of the skin showed several atypical cells, identical with those of the kidney and lungs, placed some distance above the basement membrane (fig. 8).

The meningeal space contained clotted blood. Sections of the brain showed marked edema of the cortex but no hemorrhage into the brain tissue and no hematopoietic centers. Sections of the bone marrow indicated that erythropoiesis was more marked than normal.

Blood cultures taken post mortem remained sterile.

CASE 3.—Baby R., a Negro girl, was admitted to the ward following delivery on Feb. 7, 1934. The mother had had three pregnancies. Her first child was normal, living and in good health. The second pregnancy resulted in a miscarriage

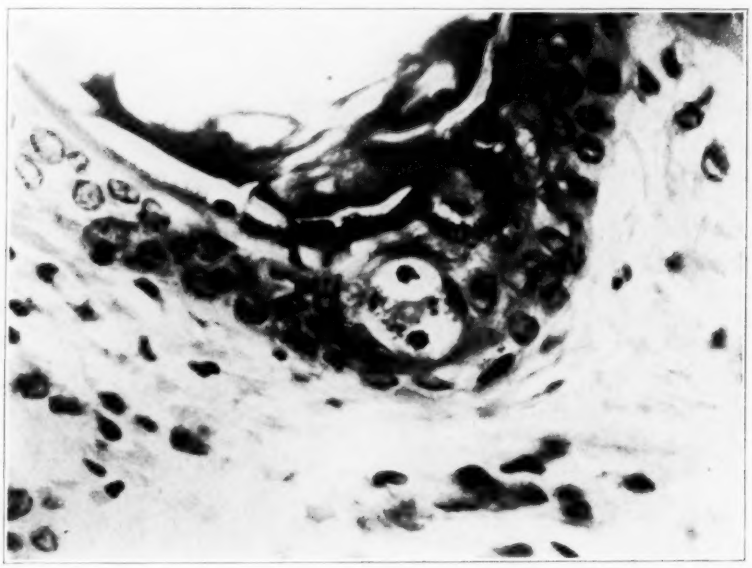

Fig. 8 (case 2).—A section of the skin showing two large atypical cells in the surface epithelium. These cells are identical with those in the kidneys and lungs.

at approximately three months, the cause of which was unknown. The mother's Wassermann reaction was negative.

The present pregnancy was entirely normal except that she had a cold in the head one month before delivery, which was approximately two weeks premature. The delivery was normal. The obstetrician noted that the placenta was larger than normal and soft and friable. He also noted that the membranes and vernix were stained golden yellow.

The baby was slightly icteric, and there was desquamation of the soles and palms. The cord was yellow. Both the liver and the spleen were enlarged. Examination of the blood revealed: 4,830,000 red cells; 83,000 total nucleated cells, of which 83 per cent were nucleated red cells, 76 per cent, neutrophilic leukocytes, 18 per cent, lymphocytes, 4 per cent, myelocytes and 2 per cent, eosinophils.

Twenty-four hours later the red blood cells numbered 3,000,000; nucleated cells, 50,000; hemoglobin, 50 per cent (Sahli), and the clotting and bleeding time were slightly prolonged. The child seemed to be in good condition.

On February 9 the red blood cells numbered 3,150,000, and there were 29,900 total nucleated cells, of which 52 per cent were nucleated red cells; the urine was yellow; the icterus index was 171; and the direct van den Bergh test showed an immediate reaction.

The following day the total nucleated cells numbered 11,450, of which 23 per cent were nucleated red cells; the blood platelet count was 175,000, and the reticulocyte count was 15 per cent. At this time 70 cc. of blood was given by transfusion, after which the patient vomited about 45 cc. of clear fluid.

On February 11, 70 cc. of blood was given by transfusion followed by a reaction similar to that noted the day before. On the next day the red blood cells numbered 5,860,000, and the hemoglobin was 76 per cent. The general condition was improved. However, on the following day the red blood cells numbered only 4,460,000, the hemoglobin was 70 per cent, and only an occasional nucleated red cell was seen. The icterus index was 75.

On February 14, eight days after delivery, no nucleated red cells could be found and the patient was gaining weight. Two days later the red blood cell count had fallen to 2,950,000, and an examination still two days later revealed only 2,870,000 red blood cells.

The condition improved steadily, and the patient was discharged on February 21, fifteen days after delivery, with a red blood cell count of 4,020,000, weighing 10¾ ounces (304.64 Gm.) above the weight at birth.

Case 4.—Baby E., a white girl, was admitted to the ward following delivery on Jan. 1, 1934. The mother came to delivery at full term following her eighth pregnancy. There had been slight bleeding during the first trimester of pregnancy and later slight hypertension. However, during the latter part of the pregnancy the condition was normal, and she came to delivery in excellent condition. The Wassermann reaction was negative. The mother had had two miscarriages, one of which was of twins. All the children were normal except the fifth child, who was jaundiced at the end of two weeks.

Ten hours after birth the patient was deeply jaundiced, the liver was 5 cm. below the costal margin, and the spleen was enlarged. No hemorrhages were noted during the stay in the hospital. The examination of the blood revealed 2,050,000 red cells; 44,300 total nucleated cells; hemoglobin, 45 per cent (Sahli); 53 per cent neutrophilic leukocytes, 35 per cent lymphocytes, 3 per cent basophils, 6 per cent myelocytes, 2 per cent monocytes, 1 per cent eosinophils, 53 per cent total nucleated red cells and bleeding and clotting time normal. Seventy-five cubic centimeters of citrated blood was given by transfusion.

On the third day of life the jaundice was increased and the number of nucleated cells was 22,000, of which 38 per cent were red cells. Transfusion of 60 cc. of citrated blood was done; the following day an additional 80 cc. was given. A rash that faded under pressure appeared over the body. The urine was yellow and contained urobilin. The icterus index was 100. The van den Bergh test showed an immediate direct reaction. The red blood cells numbered 3,430,000, and the total nucleated cells, 6,500, with 3 per cent nucleated red cells.

On the sixth day of life the baby was given 75 cc. of citrated blood by transfusion. The nucleated cells numbered 10,100, with no nucleated red cells present. On the following day 75 cc. of citrated blood was given by transfusion. Examination of the blood revealed no nucleated red cells; the white blood cells numbered 12,200, and the hemoglobin content was 85 per cent. A blood culture taken a few days prior to this was reported sterile.

On the ninth day more blood was given by transfusion. The red blood cells numbered 4,850,000, and the white blood cells, 10,150; the hemoglobin content was

80 per cent, and there were no nucleated red cells. The urine was almost green. On the twelfth day the icterus index was 300, and the direct van den Bergh test gave an immediate reaction. The next day the red blood cells numbered 4,560,000; the hemoglobin content was 62 per cent; the icterus index was 120, and the urobilin content was normal.

On the thirtieth day the child was discharged from the hospital weighing 6 ounces (170.5 Gm.) above its weight at birth. At this time the icterus index was still 70 and the direct van den Bergh test gave a delayed reaction.

COMMENT ON CLINICAL FINDINGS

The cases reported occurred in 1,958 deliveries, giving an incidence rate of 1 in 490 births. Clifford and Hertig [9] found an incidence rate of 1 to 340 in a series of 2,400 births.

The term of gestation was approximately normal except in case 1 in which the patient was born at 8 months. All the patients were girls. The condition occurs in both sexes, with a slight preponderance in boys, according to previous reports. In the cases reported by Diamond and his associates,[10] Ferguson [8] (in cases in which the sex was mentioned), Abt [11] and Buhrman and Sanford [7] nine of the patients were girls and twelve, boys.

Two of the four cases (cases 2 and 3) occurred in Negroes, and these are the first cases reported in patients of this race. The disease is believed to occur in every race and has been reported in English, Dutch, German, Scandinavian, Russian, Italian, Chinese and American children.

The patients in cases 1 and 2 were first-born children, while in case 3 the patient was the third child and in case 4, the eighth child. Clifford and Hertig [9] stated that the first-born child is usually spared. One of Abt's patients, the first born, died on the third day, after jaundice had appeared on the second day. The same condition has been reported of anemia of the new-born by Diamond and his associates and Ecklin.[13] In the first case of Buhrman and Sanford [7] there was a history of the first-born becoming jaundiced at birth, but recovering. Since two of our patients were first-born children no familial history was available. However, of the remaining two only the patient in case 4 had a familial history of jaundice, in which the child of the fifth pregnancy was noticed by the parents to be jaundiced at the end of two weeks. The disease is thought by all writers to be familial, and Abt [11] stated that the sporadic occurrence of the disease has been noted. It also occurs in twins, and in one instance de Lange [14] reported the case of one twin who had icterus gravis while the other had congenital

13. Ecklin, T.: Monatschr. f. Kinderh. **15**:425, 1919.
14. de Lange, C.: Acta pediat. **12**:292, 1932.

hydrops. Clifford and Hertig [9] suggested that a child of a subsequent pregnancy might have a different type of the disease.

Jaundice was observed in every case. In three instances jaundice was noted at birth and in one, twenty-four hours after. The patient in case 4 was markedly jaundiced while the other patients were only mildly so. This is the most constant finding; occasionally associated with it may be edema of the hands and feet.[10] Abt [11] stated that it may be present at birth and rapidly increase during the first hours of life. It is unusual for the jaundice to appear later than the first twenty-four hours, which helps to differentiate it from benign icterus.

Generalized petechiae were observed in two instances, and in one ecchymoses were noted. Both conditions were more pronounced on the upper part of the body. Three patients had no rash, while on the fourth day the patient in case 4 had an erythematous rash that faded under pressure, which was probably a reaction to the transfusion of blood. The only external bleeding noted was in case 2, in which the patient died of pulmonary hemorrhage. Since this happened while blood was being transfused it should not be attributed to the disease, for it is probable that the transfusion precipitated the hemorrhage. This tendency to bleed is present in about half the cases, according to Clifford and Hertig.[9] More extensive bleeding may develop within a few days.

The spleen was enlarged in all the cases except one, in which no note was made of the size of the spleen. At autopsy in case 2 the spleen was found to be greatly enlarged, weighing 40 Gm., which was estimated to be four times normal weight.[15] The liver was palpable in one of our cases; the size was not recorded in one and was considerably enlarged in the other two.

The most important clinical data are the hematologic observations. We give the average values for the blood of infants, as reported by Holt,[16] for comparison: The red cell count at birth is 5,500,000, while at the end of the sixth day it is 5,000,000 and at the twelfth day, 4,800,000. At birth the white blood cell count is 20,000; it falls to 13,000 at the third day, while at the tenth day it is 12,000. The reticulocyte count at birth is 2.5 per cent, while by the tenth day it falls to 1 per cent. Lippman [17] gave the normal average for nucleated red cells at birth as 5 per cent, the value falling to 1 per cent by the second day.

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15. Griffith J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1933, p. 44.

16. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton & Company, 1933, p. 529.

17. Lippman, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

The anemia found in these infants was not uniformly as profound as in cases previously reported. In every case the red cell count was below the average except in the first count in case 1 and on that reported on the sixth day in case 3, but the patient in the latter case had received 70 cc. of blood on each of the two preceding days. All the patients received fairly large amounts of blood at frequent intervals. This may account for the anemia not becoming so marked. This may also account for the color index not remaining consistently above unity as is usually the condition. In every instance the red cell count was above 2,000,000.

The abnormal red blood cells varied from the early erythroblasts to normoblasts. Basophilic red cells were found. The nuclei of numerous early erythrocytes showed mitotic figures (fig. 1). The red cells showed marked changes in shape but relatively little change in size. The immature and nucleated red cells were the outstanding observations. They were numerous in every instance, with a tendency (in the patients who recovered) to disappear from the blood stream after six or seven days. In one patient the total count for the abnormal primitive red cells was 83 per cent of the total nucleated cells.

There was a tendency toward leukocytosis, with an increased number of granulocytes which later became normal in the patients who survived. There was also slight eosinophilia in the latter days of the disease. Immature cells of the myeloid series were found.

The platelets were recorded only in cases 1 and 3 and only once in each. In the former the count was 270,000, and the patient bled, while in the latter the count was only 175,000, but the patient did not bleed. Early in cases 1, 2 and 3 there was a prolonged clotting and bleeding time, but not so in case 4. The bleeding and clotting time became normal in a relatively early stage of the disease in all three.

The icterus index was high in all and became lower as the patients began to recover. There was an immediate reaction to the direct van den Bergh test. The laboratory did not report the reaction to the indirect test, however. In the cases previously reported by other authors both reactions have been positive.

Blood cultures were made in cases 2 and 4, and in both the cultures were reported sterile. The Wassermann reaction of each of the mothers was negative.

SUMMARY

Four cases of erythroblastosis in which two of the patients recovered and one came to autopsy are reported. Two of the patients were Negroes; these are the first cases of the disease to be reported in the Negro race. The incidence was 1 in 490 in a review of 1,958 births. Three patients had a normal period of gestation and one was premature. Two were first born. All were girls. In one case there was a familial

history of jaundice, and all the patients were jaundiced during the course of the disease. Hemorrhages appeared in two. The spleen was enlarged in all the patients, and the liver was enlarged in two. There was anemia in all, but no red blood cell count was below 2,000,000. There were many nucleated red cells and a tendency toward leukocytosis, the latter condition disappearing in the patients who recovered. Cells of the myeloid series varied from 1 to 8 per cent, and the color index was near 1 in all cases.

Postmortem examination revealed many hematopoietic centers in the liver, kidneys, spleen and pancreas. Hemorrhages were numerous throughout the body, especially in the lungs. In the kidneys, lungs and skin were large atypical epithelial cells, an explanation of which is lacking. The bone marrow was moderately hyperactive.

RENAL CALCULI IN AN INFANT

COMPLICATED BY PERINEPHRITIC ABSCESS AND SUBARACHNOID HEMORRHAGE

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BRONX, N. Y.

Renal calculi undoubtedly cause greater morbidity in children under 2 years of age than the reports of their incidence suggest. The case to be presented is the sixteenth on record in all the literature in which a clinical diagnosis of a renal calculus over 3 mm. in diameter was made on an infant.[1] In contradiction to this apparent rarity are the reports collected from the most recent literature [2] showing the relatively high incidence of 0.05 per cent among 9,323 infants who came to necropsy. Other observers who included patients with gravel and smaller stones have had even greater incidence.[3] If in addition to this one considers the number of cases of nephrolithiasis diagnosed during later life with

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From the Pediatric Service of the late Dr. William L. Rost, Morrisania City Hospital.

1. (*a*) Butterfield, P. M.: Urology in Children, Am. J. Surg. **10**:358, 1930. (*b*) Campbell, M. F.: Urinary Calculi in Infancy and Childhood, J. A. M. A. **94**:1753 (May 31) 1930; Renal Calculi in Infancy and Childhood, Am. J. Dis. Child. **40**:451 (Aug.) 1930. (*c*) Charvin, E.: De la lithiase rénale et urétérale chez l'enfant; forme chirurgicale, Thesis, Lyons, 1911. (*d*) Collins, A. N.: Urinary Lithiasis in Infancy, Am. J. Dis. Child **6**:245 (Oct.) 1913. (*e*) Deherripon, H.: Lithiase rénale chez un nourrisson de trois mois, Bull. Soc. pédiat. de Paris **25**:460, 1927. (*f*) Hill, M. C., and Stevens, A. R.: Nephrolithiasis in a Girl of Three Years, Arch. Pediat. **37**:615, 1920. (*g*) Hinman, F.: Multiple Renal and Ureteral Stones in an Infant of Eleven Months, J. A. M. A. **76**:237 (Jan. 22) 1921. (*h*) Lowsley, O. S., and Butterfield, P. M.: Urological Conditions Among Children, J. Urol. **16**:415, 1916. (*i*) Monsseaux, A.: Sur la lithiase rénale chez les enfants, Rev. mens. d. mal. d. l'enf. **22**:205, 1904. (*j*) Rafin: De la lithiase rénale et urétérale chez l'enfant, Ann. d. mal. d. org. génito-urin. **29**:481, 1911. (*k*) Thomas, G. J., and Tanner, C. O.: Urinary Lithiasis in Children, J. Urol. **8**:171, 1922. (*l*) Ulmer, O.: Lithiasis im frühesten Kindesalter, Arch. f. Kinderh. **85**:87, 1928. (*m*) Wiles, P.: Renal Calculi in Infants, Lancet **2**:794, 1930.

2. Bugbee, H. G., and Wollstein, M.: Surgical Pathology of the Urinary Tract in Infants, J. A. M. A. **83**:1887 (Dec. 13) 1924. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1918, p. 520. Campbell.[1b]

3. Lignac, G. O. E.: Over niersteenvorming bij kinderen in het erste levensjaar, Nederl. tijdschr. v. geneesk. **1**:3084, 1929. Comby, T.: Lithiase rénale chez les enfants, Arch. de méd. d. enf. **2**:577, 1899.

vague symptoms dating back to infancy,[4] one is compelled to assume that a number of cases in infants are not recognized.

Renal lithiasis must be considered in all cases of repeated or prolonged abdominal pains without diarrhea and of persistent pyuria or in the presence of hematuria, frequency or oliguria. The symptomatology resembles that in adults and may be readily confused with gastrointestinal dysfunction or pyelonephritis. Unless the syndrome is kept in mind and appropriate diagnostic procedures instituted, cases will be repeatedly diagnosed incorrectly. With the more widespread use of roentgenography, intravenous urography and cystoscopy of infants the correct diagnosis should be made more frequently.

The following case is one of the very few on record in which the correct diagnosis was made during the life of an infant and subsequently proved by autopsy. It is also of interest because of the unusual complications.

REPORT OF CASE

G. W., a girl, entered the Morrisania City Hospital on March 18, 1933, at the age of 14 months because of oliguria. Her weight was 14 pounds and 15 ounces (6,775.53 Gm.). She was born following a seven month gestation weighing 4 pounds and 14 ounces (2,211.27 Gm.); the delivery was normal. There was no history of illness, although the child was always pale and anoretic, until two months prior to admission, when she first began to urinate more frequently and in greater quantity than previously. This persisted until four days prior to admission, when, associated with fever, oliguria and dysuria set in. This became progressively worse, so that on admission she was screaming and tossing about with pain, continually dribbling a few drops of thick urine and scratching the vulva.

The infant appeared chronically ill and pale. The head was asymmetrical, the pharynx was injected and both ear drums were retracted. Ophthalmoscopic and neurologic examinations revealed no abnormalities. The vulva was red and irritated. The abdomen was soft and the liver palpable. A firm, tender mass was palpable in the left flank; this extended 2 inches (5 cm.) below the costal margin and did not move on respiration. A catheterized specimen of urine obtained on the patient's admission to the hospital was alkaline, having a specific gravity of 1.030 and containing albumin (++), occasional casts and 14 white blood cells

4. Brown, D. A.: Renal and Ureteral Calculi in Childhood, J. Urol. **18**:285, 1927. Keyes, E. L., Jr.: Urinary Calculi, Am. J. M. Sc. **161**:334, 1921. Charvin.[1e] Hill and Stevens.[1f] Konig, F.: Zur Entstehung von Nierensteiner in den ersten Lebenswochen, München. med. Wchnschr. **69**:1426, 1922. Monsseaux.[1i] Nash, W. G.: Two Cases of Renal Calculus in Children Under Ten Years, Rep. Soc. Study Dis. Child., London **6**:186, 1906. Ollerenshaw, N.: Renal Calculi in Childhood, Brit. M. J. **1**:112, 1913. Porter, M. F.: Stone in the Bladder of a Female Child of Four Years, Ann. Surg. **34**:819, 1901. Rafin.[1j] Simons, S.: Twee gevallen van nephrolithiasis bij kinderen, Nederl. tijdschr. v. geneesk. **1**:1290, 1926. Thomas, G. J., and Rodda, F. C.: Multiple Cystine Calculi in the Left Kidney with Obstruction at the Ureteropelvic Juncture and Multiple Cystine Calculi in the Bladder of a Boy of 4 Years, Journal-Lancet **51**:538, 1931. Thursfield, H.: Diagnosis of a Case of Renal Calculus in a Child, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **14**:95, 1920-1921.

and 40 red blood cells per high power field. The blood count revealed 10,200 white blood cells with 76 per cent polymorphonuclear leukocytes and 24 per cent lymphocytes. There were 2,800,000 red blood cells with 15 per cent hemoglobin (Dare). The blood pressure was 104 systolic and 70 diastolic.

Roentgen examination of the urinary tract (fig. 1) revealed a large single dense shadow (calculus) in the position of the left kidney and two others in the region of the right kidney, and a subsequent film (fig. 2) showed, in addition, a mass in the left lumbar region, which appeared to be distended kidney.

The condition was diagnosed as bilateral renal calculi with pyonephrosis on the left side.

The general condition grew progressively worse. In spite of repeated clysis, attempts at acidification of the urine and high hot colonic irrigations, she voided

Fig. 1.—Roentgenogram showing a large single dense shadow (calculus) in the position of the left kidney and two others in the region of the right kidney.

only a few cubic centimeters of urine during the twenty-four hours. On March 26, she appeared very toxic and had twitchings of the left hand, which were attributed to uremia. Owing to the moribund condition of the child, cystoscopy was deemed inadvisable. A transfusion by the citrate method was given on March 27, during which procedure the mass in the left flank became more tense, so that it was about the size of a large orange, very tender and fluctuating. Incision and drainage of the mass under local anesthesia were performed, yielding 200 cc. of pus. The cavity was explored, and its boundaries were thought to be a shell of the renal tissue. The patient died two hours after operation.

Necropsy.—Lungs: On gross examination, no abnormality was noted, but the microscopic sections revealed an interstitial bronchopneumonia.

Heart: There were no abnormal findings.

Abdominal Cavity: On the left side, there was a large sac about 4 inches

long, 2 inches wide and 1½ inches deep (10 by 5 by 3.8 cm.), into which drains had been inserted through a surgical wound. The right wall of this sac was the true capsule of the kidney. The lateral walls were formed by intimate adhesions of the wall of the sac to the peritoneal surfaces of the descending colon and spleen. This sac communicated with a dilated calix through a perforation in the upper pole of the kidney. On section of the kidney the dilated calix was seen to have a thickened yellow wall with a calculus partially obstructing its outlet. The kidney itself was pale, with numerous whitish striae and nodules on the surface, which on microscopic examination were found to be abscesses. The other calices were

Fig. 2.—Roentgenogram showing, in addition to the findings in figure 1, a mass in the left lumbar region, which appeared to be distended kidney.

lined with a yellow stonelike material. The left ureter was dilated, and it contained a stone, oval in shape, 2¾ inches long and ½ inch in diameter (1.27 cm.), and several smaller conglomerations of gravel. The renal pelvis also contained conglomerations of gravel. On the right side, the ureter was dilated and thickened, and it contained several fine yellow stones. Yellow stones were present in two of the calices, one of which was about 1½ by ¾ by ½ inches (3.8 by 1.9 by 1.3 cm.) and was an exact cast of the calix.

Microscopic studies of the sections of the kidneys showed: 1. The interstices were infiltrated irregularly with polymorphonuclear cells, which in some areas

formed small abscesses. This process was especially intense in the cortex. 2. There were no changes in the glomeruli. 3. The tubules were necrotic in the abscessed areas and some cloudy swelling in outside areas. 4. There was slight thickening of the media of the small arteries by hyalin.

Diagnosis: The condition was diagnosed as pyelonephritis.

Bladder: The bladder was slightly contracted, and the wall definitely thickened. A large number of small, yellowish stones, some hard and others soft, were present.

Liver: The liver was slightly enlarged and appeared yellow on section. Sections showed cloudy and fatty degeneration.

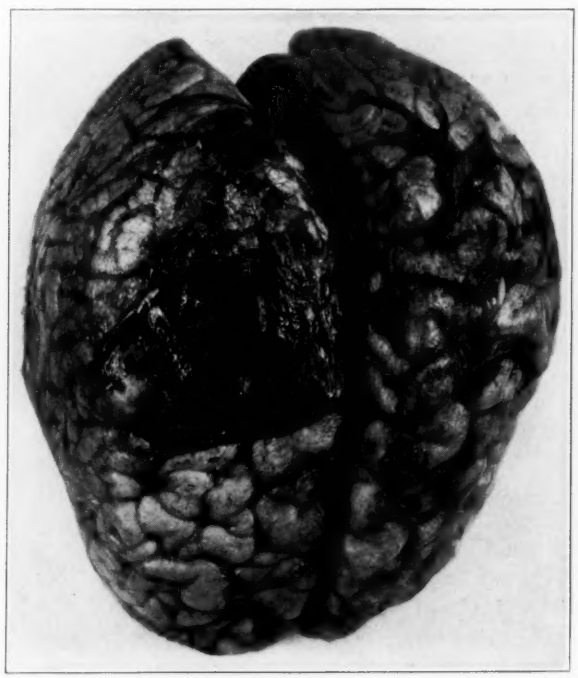

Fig. 3.—External view of the brain. The veins on the convex surface are markedly engorged, particularly over the right side. There is, in addition, a subarachnoid hemorrhage on this side, extending from the precentral to the postcentral area and into the gray and white matter.

Spleen: The spleen was slightly enlarged and purplish and firm on section, showing hyperplasia of the reticulo-endothelial cells of the pulp which was found on study of the retroperitoneal lymph nodes.

Chemical analysis of the stones revealed calcium oxalate, uric acid and phosphates. Pus cultured from the perinephritic abscess showed Staphylococcus aureus and Bacillus coli.

Head (fig. 3): On removal of the calvaria, it was noted that the veins on the convex surface of the brain were markedly engorged, particularly over the right side. There was, in addition, a subarachnoid hemorrhage on this side,

extending from the precentral to the postcentral area and into the gray and white matter. On removing the dura from the calvarium there was seen an area of pus surrounding the superior longitudinal sinus at the junction of the parietal and the occipital bones, which on smear did not show any organisms.

The superior longitudinal sinus was found to be intact, while both lateral sinuses were thrombosed. Pus was found in both mastoids, which, on examination, showed short-chained streptococci and staphylococci. Hemolysis was noted on the blood plate.

A section of the lateral sinus showed an infectious thrombus consisting of polymorphonuclear leukocytes, débris, blood pigment and beginning organization.

A coronal section of the right hemisphere revealed a subarachnoid hemorrhage over the superior portion of the parietal lobe which destroyed the architectural layers of the cortical convolutions. The veins in the subarachnoid space were distended and filled with red blood cells and blood pigment. The hemorrhage extended into the white matter. In addition to the gross hemorrhage there were collections of inflammatory cells surrounded by rings of hemorrhage. In some places, there was deposition of fibrin and proliferation of microglia cells. Most of the ganglion cells were of the ischemic type. However, chronic and severe changes were noted. In other areas, the meninges were thickened and filled with inflammatory cells. The cortical areas bordering these showed proliferation of the vessels, surrounded by inflammatory cells. The ganglion cells showed changes similar to those mentioned. There was also proliferation of microglia cells in these areas.

Anatomic Diagnosis: The diagnosis was (1) multiple bilateral renal and ureteral calculi, (2) perinephritic abscess on the left side resulting from the rupture of a dilated pyonephritic calix; (3) pyelonephritis; (4) interstitial bronchopneumonia; (5) cloudy and fatty degeneration of the liver; (6) acute hyperplastic spleen and lymphadenitis; (7) bilateral mastoiditis; (8) infectious thrombosis of the lateral sinus; (9) subarachnoid hemorrhage; (10) meningitis; (11) encephalitis.

COMMENT

Reviewing the case, one notes the advanced changes in the kidney and the early onset of symptoms, facts which lead one to classify the condition as probably of congenital origin. However, definite urinary symptoms did not manifest themselves until the child was 12 months of age. Had the diagnosis been established at this time and adequate treatment instituted, the complications might have been avoided. Two months later, when the patient was first admitted to the hospital, there was already severe impairment of renal function, with urinary obstruction and with a perinephritic abscess originating from a perforated pyonephrotic calix.

Another phase of the case which is of interest is the findings in the brain and skull. A day prior to death, twitchings of the left hand developed, which were interpreted as of uremic origin. However, the postmortem examination revealed a subarachnoid hemorrhage involving the right motor area of the brain, probably due to rupture of an infected blood vessel which extended into the brain substance. There was, in addition, an extension of the inflammation into the parenchyma of the

brain, which gave rise to meningo-encephalitis. These processes all originated from infectious thrombosis of the lateral sinus which, in turn, was probably due to an extension from a latent mastoiditis. It is interesting to note that during life repeated otologic examination failed to show any involvement of the middle ear and yet, on postmortem examination, there was an extensive mastoiditis.

I believe that the mastoiditis, however, had no direct relation to the renal infection but that owing to general toxemia and reduced resistance an infection of the middle ear and mastoiditis developed. This, in turn, gave rise to thrombosis of the lateral sinus and inflammation of the meninges, blood vessels and brain cells. There is no definite proof that the thrombosis of the sinus and the cerebral infection were not metastases from the kidney, except that none of the other organs showed evidence of pyemia. However, Staphylococcus ureae was recovered from both the mastoids and the kidney, in addition to the other organisms.

SUMMARY

The case reported is the sixteenth on record of renal calculi in an infant diagnosed during life. It is also of interest because of the presence of a perinephritic abscess and a subarachnoid hemorrhage, neither of which has been reported as a complication of renal calculi in infants.

SEPTICEMIA DUE TO ESCHERICHIA ACIDI-LACTICI (BACILLUS ACIDI-LACTICI) IN A NEW-BORN INFANT

REPORT OF A CASE WITH NECROPSY

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Three cases of meningitis in new-born infants caused by Bacillus acidi-lactici have been reported by Greenthal,[1] Sherman [2] and Pasachoff.[3] None of these observers mentioned whether the infants had a positive blood culture. Ray [4] reported the case of a man, aged 55, who had a retroperitoneal abscess, mediastinitis, pleurisy and pneumonia. A blood culture showed B. acidi-lactici, and a spinal fluid culture showed the same organism on two occasions.

Dickar [5] reported two cases of endocarditis due to B. acidi-lactici. One patient, a man of 54, had a prostatic abscess, which was incised and drained. Later subacute bacterial endocarditis developed. At autopsy a pure culture of B. acidi-lactici was recovered from the blood of the heart, and evidences of metastases due to bacteremia were shown in the myocardium, pancreas, liver, kidneys, testes, brain and meninges. Dickar's second patient, a woman of 63, was admitted to the hospital with the complaint of chills, fever and nausea. A blood culture showed B. acidi-lactici. Physical examination and roentgenograms showed an enlarged heart, and a loud systolic murmur was heard at the apex. At autopsy there were observed acute gangrenous cholecystitis (B. acidi-

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1. Greenthal, R. M.: Case of Meningitis Due to the Bacillus Acidi-Lactici, Am. J. Dis. Child. **21**:203 (Feb.) 1921.

2. Sherman, DeWitt: A Peculiar Case of Purulent Meningitis in the New-Born, Tr. Am. Pediat. Soc. **34**:192 (May) 1922.

3. Pasachoff, H. D.: Meningitis Due to Bacillus Acidi-Lactici in a New-Born Infant, Am. J. Dis. Child. **41**:862 (April) 1931.

4. Ray, H. M.: A Fatal Case of Bacillus Acidi-Lactici Meningitis, J. Lab. & Clin. Med. **8**:260 (Jan.) 1923.

5. Dickar, L.: Acute Bacterial Endocarditis Due to Bacterium Acidi-Lactici, Arch. Int. Med. **49**:788 (May) 1932.

lactici) and acute endocarditis (B. acidi-lactici). Dunham,[6] in her report of thirty-nine cases of septicemia in new-born infants, discussed ten cases of septicemia due to Bacillus coli. In six of these B. acidi-lactici was definitely ruled out. In the remaining four it is possible that B. acidi-lactici was present, for it was not ruled out.

As far as we can determine, the following report of a case is the only one which records a positive infection in the blood stream with B. acidi-lactici in a new-born infant. As Ray pointed out, it is possible that infections from B. acidi-lactici in man may have been present among the reported cases of suppurative meningitis, since reactions on the various carbohydrates were not recorded. In order to determine whether the organism in question is Bacillus coli-communis, Bacillus coli-communior, Bacillus aerogenes or B. acidi-lactici, a study of its fermentation reactions with various carbohydrates is necessary. The cultural characteristics of B. acidi-lactici are fermentation of dextrose, lactose, maltose and mannitol but absence of fermentation of sucrose, dulcite and salicin. The report of the case follows:

REPORT OF CASE

History and Course.—H. A., a boy, was born on Dec. 13, 1933, at the Sloane Hospital by cesarean section. The section was done because the mother had had several abdominal operations.

The infant's weight was 3,120 Gm. at birth, and his condition was good. His course was uneventful until the thirteenth day, when his temperature rose to 100.2 F. This rise was not explained. His weight at this time was 120 Gm. below his weight at birth. He had not been breast fed but had been put on a formula of diluted whole milk and dextrimaltose. When he was 16 days old, his temperature rose to 101.4 F. Circumcision was performed on this day. The temperature was moderately high and irregular for the next seven days (until Jan. 3, 1934).

A pediatric consultation was requested on Dec. 29, 1933. The positive findings on physical examination were: moderately injected ear drums and a recent circumcision wound, which did not appear infected. The hemoglobin was 11.6 Gm. (73 per cent, Sahli) per hundred cubic centimeters. The red cell count was 3,800,000 per cubic millimeter. The white cell count was 12,000 with 58 per cent polymorphonuclear leukocytes.

On December 31 the infant appeared acutely ill. The right ear drum was injected. Both kidneys were slightly enlarged and possibly tender. The urine showed gross pyuria. A transfusion of 45 cc. of whole blood was given on account of the anemia, using the father as donor.

On Jan. 2, 1934, the hemoglobin was 14.4 Gm. (90 per cent, Sahli) per hundred cubic centimeters, and the red cell count was 4,300,000 per cubic millimeter. The ear drums were still injected, but there was no bulging.

On January 3 a blood culture showed Escherichia acidi-lactici (B. acidi-lactici). The urine again showed gross pyuria. A transfusion of 50 cc. of whole blood was given, using the father as donor.

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6. Dunham, E. C.: Septicemia in the New-Born, Am. J. Dis. Child. **45**:229 (Feb.) 1933.

On January 4 the patient was transferred to the Babies Hospital. His weight was 3,010 Gm. The temperature for the remaining eight days of life was only twice between 101 and 102 F. and was below 101 F. the rest of the time. It was subnormal for the last twenty-four hours of life, reaching 93.6 F. at its lowest point.

Bacteriophage prepared from the organism recovered from the blood stream was given. Two and five-tenths cubic centimeters of undiluted phage was given in 50 cc. of saline solution intravenously, and 2.5 cc. was also given in the formula. A second blood culture was positive for B. acidi-lactici. The white cell count was 29,000, with 65 per cent polymorphonuclear leukocytes. Microscopic examination of the urine showed many leukocytes, occurring singly or in clumps, in every high power field.

From January 5 to January 12 the course was steadily downhill, with a final weight of 2,540 Gm. There was diarrhea, and vomiting of coffee-ground material occurred as a terminal picture.

On January 10 the third and last blood culture showed no growth.

On January 11 transfusion of 50 cc. of blood was given. Bacteriophage (2.5 cc.) was given intravenously in saline solution. On the last day of life all the tissues of the body showed sclerema.

Death occurred thirty-one days after birth and fifteen days after the onset of the illness. The clinical diagnosis was: (1) septicemia due to B. acidi-lactici, (2) pyelonephritis due to B. acidi-lactici and (3) sclerema neonatorum.

Necropsy.—Macroscopic Examination: Necropsy was performed seventeen and a half hours after death. The body was that of a normally developed, emaciated, white infant, measuring 50 cm. in length. The skin of the cheeks and of the lateral surface of the thighs and upper arms was stiff and waxlike in consistence. There was no discharge from the ears. The abdomen was moderately distended, and the skin of the scrotum was rough and slightly red, but the circumcision wound was healed.

The peritoneal surfaces were free from exudate, and there were no evidences of inflammation on the posterior surface of the umbilicus or in or about the umbilical vein or the hypogastric arteries.

Both pleural cavities were normal. The thymus was small. The pericardial sac contained several cubic centimeters of clear, straw-colored fluid.

The heart weighed 20 Gm. On the infundibular leaflet of the tricuspid valve and on both leaflets of the mitral valve were tiny angiomatoid nodules. The foramen ovale was patent.

The aorta was normal. The ductus arteriosus was pervious.

The thymus weighed 2 Gm. On section the lobules were small and pale pink.

The mucosa of the epiglottis, trachea and main bronchi was injected.

The left lung weighed 46 Gm. Most of the pleura was free from exudate, but over the posterior and diaphragmatic surfaces of the lower lobe the normal pleural gloss was absent, and the surface was dull. On section both lobes contained small, deep red, firm, slightly elevated areas. In the lower lobe there was confluence of some of the consolidated regions, and tiny, yellow flecks were visible. The cut surfaces of both lobes were moist.

The right lung weighed 54 Gm. and was similar in its main features to the left lung. The pleura in places was covered by thin, granular exudate.

The spleen weighed 6 Gm. and was moderately soft. It was deep red, and the malpighian bodies were not visible.

The liver weighed 128 Gm. The organ was brownish red and free from abscesses and phlebitis.

The lower end of the esophagus was slightly congested; the gastric mucosa showed no ulcers, and the small and large intestine were normal.

The adrenals were normal.

The right kidney, with the capsule attached, weighed 25 Gm. The capsule stripped readily, disclosing a brownish red surface extensively mottled with irregular, yellowish-gray areas, measuring up to 1.5 cm. in diameter. These regions, often confluent, formed over the surface of the kidney an irregular grayish pattern, in which a few opaque, yellow points were visible. The kidney was soft. On section yellowish-gray streaks radiated through the medulla and cortex. The pelvis was not dilated, and no exudate was seen on the mucosa.

The left kidney weighed 20 Gm. It was, in general, similar to the right, though the pathologic changes were less widespread. The pelvis on this side also was normal.

The ureters were of average size and free from exudate.

The bladder and urethra were normal. There was no inflammation about the circumcision wound. The large veins of the penis were dilated and filled with dark red blood clots, which were not attached to the walls of the vessels. The testes were normal.

Each middle ear contained thick, yellow exudate, in which staphylococci were demonstrated with the Gram stain.

The dural sinuses of the brain contained no thrombi; the pial vessels were congested. The cavum septi pellucidi was mildly dilated, but the brain was otherwise normal.

B. acidi-lactici was recovered from cultures of material taken from the kidneys.

Microscopic Examination: In radiating, wedge-shaped areas, extending through the cortex and pyramids of the kidneys there was heavy infiltration of the renal structures by polymorphonuclear and mononuclear leukocytes. In such regions in the cortex occasional tubules were still lined by degenerating epithelial cells, but in most the lumens were filled with cellular exudate. In small abscesses in the cortex were numerous short, gram-negative bacilli, and large numbers of similar organisms appeared in the capsular spaces, in the tubular lumens and in the cytoplasm of many of the polymorphonuclear leukocytes. In the pyramids the collecting tubules were dilated by large accumulations of inflammatory cells. The interstitial tissue was edematous and infiltrated with leukocytes; occasional capsular spaces were filled with polymorphonuclears, and between the collecting tubules were many small hemorrhages. The epithelium lining the pelvis was still preserved, though the cavity of the pelvis contained a small amount of purulent exudate.

In many of the pulmonary lobules was a widespread pneumonic exudate, in which leukocytes were degenerating; many hemolyzed erythrocytes were present, and there were huge masses of bacteria, most of which were staphylococci, though a few gram-negative bacilli appeared also. The bronchi were filled with purulent exudate, erythrocytes and myriads of staphylococci.

In the epithelium of the larynx were foci in which there was necrosis of cells, with clumps of staphylococci entangled in the epithelial débris. The subjacent connective tissue was edematous and infiltrated with fibrin and leukocytes.

The spleen contained heavy deposits of iron.

In many of the hepatic cells were large and small vacuoles of fat, and occasional bile radicles were dilated by small plugs of bile. In many of the Kupffer cells and in some of the liver cells iron-containing pigment was demonstrable.

The lobules of the thymus were small; the cortex was depleted of lymphocytes, and large pale cells were numerous in the depleted areas. Moderate numbers of eosinophils occurred in the gland.

Sections from the penis failed to show inflammatory changes in the region of the circumcision scar, and the large veins were free from thrombi or phlebitis. Sections from the umbilicus, umbilical vein and hypogastric arteries were normal.

The anatomic diagnoses were: acute suppurative nephritis (B. acidi-lactici); septicemia (B. acidi-lactici); acute laryngitis; lobular pneumonia (staphylococcus); acute fibrinous pleurisy; acute purulent otitis media (staphylococcus); edema of the lungs; sclerema; accidental involution of the thymus; angiomatoid nodules on the tricuspid and mitral valves; hemosiderosis of the liver and spleen; patent foramen ovale; patent ductus arteriosus; dilated cavum septi pellucidi.

COMMENT

In the two adult patients with B. acidi-lactici bacteremia whose cases were reported by Dickar the initial portals of entry of the organism into the blood stream were a prostatic abscess and gangrenous cholecystitis, followed by localization of the bacilli on the aortic valves. In the reported cases of meningitis due to B. acidi-lactici in early infancy the initial focus was not so readily determined, though the possibilities of intra-uterine infection, bacterial invasion from a circumcision wound or infection of the nasopharynx or ears, with subsequent involvement of the meninges, were mentioned by Pasachoff. In the case presented here bacillemia may well be explained as an invasion of the blood stream by B. acidi-lactici from the suppurative renal lesions, though the route by which the organisms reached these organs is unproved. Felty and Keefer,[7] in a series of cases of sepsis due to the colon bacillus in older children and adults, found a urinary infection in sixteen of twenty-five patients, occurring in some of the older men following prostatic obstruction. In our case, however, there was no congenital anomaly of the urinary tract to produce urinary obstruction and the absence of cystitis, ureteritis and pyelitis suggests that the renal lesions were not the results of an ascending suppurative process.

There is no evidence in the mother's medical history to support the view of an intra-uterine origin of the infection, and the postmortem studies failed to reveal an inflammatory process of the umbilicus and related intra-abdominal vessels or of the circumcision wound. In addition the presence of fever prior to the operation rules out the probability of infection from the site of circumcision. While infection of the middle ears by B. acidi-lactici cannot be excluded conclusively in this case, the masses of cocci in the exudate tend to link the suppurative otitis media observed at necropsy with the acute laryngitis and pneumonia, in which the staphylococcus was the predominating organism. A more probable source for B. acidi-lactici would seem to be the gastro-intestinal tract of the patient, though no lesion in the stomach or the intestine was noted to corroborate this conclusion.

7. Felty, A. R., and Keefer, C. S.: Bacillus Coli Sepsis, J. A. M. A. **82**: 1430 (May 3) 1924.

SUMMARY

A case of septicemia due to B. acidi-lactici in a new-born infant is presented.

Although cases of septicemia due to Bacillus coli are not uncommon in the new-born infant, we believe that this is the first case in which this member of the group (B. acidi-lactici) has been differentiated and demonstrated in the blood stream as early as the twenty-first day of life.

Observations at necropsy indicated that the organism had gained access to the blood stream by way of the kidneys, where suppurative nephritis was present.

Progress in Pediatrics

CLINICAL AND ANATOMIC STUDY OF AVITAMINOSIS A AMONG THE CHINESE

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The fat-soluble factor, vitamin A, although not yet isolated in pure form and although totally unknown until the last decades, has held the attention of clinicians, through the manifestations of its deficiency, since the earliest times. Night blindness, one of the first symptoms of avitaminosis A, was known to Hippocrates, and the beneficial results of a liver diet in the treatment of this disorder were described by Paul of Aegina.[1] The more advanced symptom complex, keratomalacia, was not described until the middle of the last century, however, Brown [2] in 1827 and Fischer [3] in 1846 being credited with having given the first descriptions. Arlt [4] in 1851 also described the condition, and in 1862 Bitot [5] linked hemeralopia with xerosis of the conjunctivae. Complete descriptions of the disease were first given by da Gama Lobo [6] in 1864 and by von Graefe [7] in 1866. The relationship of keratomalacia to vitamin A deficiency was demonstrated conclusively by Bloch,[8] who was one of the first to stress that the disease is one characterized by general manifestations of which the ocular symptoms are only a part.

Since the disease has become known generally, many authors have combined to amass a voluminous literature on vitamin A itself and on

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1. Holcomb, R. C.: Night Blindness, J. A. M. A. **102**:786 (March 10) 1934.
2. Brown, J., quoted by Mackay.[65]
3. Fischer, J. N., quoted by Blegvad.[10]
4. Arlt, C. F.: Die Krankheiten des Auges, Prague. F. A. Credner & Kleinbub, 1854, vol. 1, p. 211; quoted by Blegvad.[10]
5. Bitot: Mémoire sur une lésion conjonctivale non encore décrite, coïncidant avec l'héméralopie, Bull. Acad. de méd., Paris **28**:619, 1862.
6. da Gama Lobo, M., quoted by Ullersperger, B.: Brasilianische Augenentzündung, Monatsbl. f. Augenh. **4**:65, 1866.
7. von Graefe, A.: Hornhautverschwärung bei infantiler Encephalitis, Arch. f. Ophth. **12**:250, 1866.
8. Bloch, C. E.: Clinical Investigation of Xerophthalmia and Dystrophy in Infants and Young Children, J. Hyg. **19**:283, 1921; Blindness and Other Diseases in Children Arising from Deficient Nutrition (Lack of Fat-Soluble A Factor), Am. J. Dis. Child. **27**:139 (Feb.) 1924.

the manifestations of its deficiency. The articles have dealt primarily with experimental problems, or they have been studies made by ophthalmologists. Studies from the point of view of the internist and pathologist have been few indeed, and there have been no attempts to correlate the general symptomatology and the pathology. We have studied the records of 203 patients suffering from various manifestations of avitaminosis A and the material obtained from 17 necropsies and 19 specimens taken for biopsy from conjunctiva, skin and 3 enucleated eyeballs. All the patients were admitted to the wards of the Peiping Union Medical College Hospital between the years 1921 and 1934. They were admitted in various services. If lesions of the eye were present, they were diagnosed by some member of the ophthalmological service. There was a free use of medical and ophthalmologic consultations on almost all cases. The pathologic material is that obtained by routine autopsies and specially performed biopsies. Many of these cases have been reported before and form the basis for communications from this clinic by Hsu, Pillat, John, Keefer, Chou, Frazier, Weech and their associates.

Before entering on a discussion, it is well to emphasize the fact that, unlike experimental animals on well controlled diets, these patients were almost always suffering from multiple deficiencies. Wu and Wu [9] demonstrated that the average Chinese diet, while supplying adequate fuel value and usually adequate vitamins B and C, contains suboptimal amounts of protein and vitamins A and D and is deficient in calcium and phosphorus. The patients in this series either were on diets far below the average or were suffering from pathologic conditions which prevented the full utilization of their food. And, as will be seen later, many of them had well developed evidence of other deficiency diseases. Consequently we are unable to draw definite conclusions about which of the changes noted in this study actually are due to deficiency of the fat-soluble A factor and which to associated disturbances. As keratomalacia or xerophthalmia was a prominent feature in each of the cases, however, and as the general symptoms usually are not associated with other known deficiencies, they are assumed to be due in large part to the lack of vitamin A.

ETIOLOGY

The age incidence of these patients is of considerable interest. Blegvad [10] and others stated that keratomalacia is a disease of early

9. Wu, H., and Wu, D. Y.: Study of Dietaries of Peking, Chinese J. Physiol. **1**:135 (July) 1928.

10. Blegvad, O.: Xerophthalmia, Keratomalacia and Xerosis Conjunctivae, Am. J. Ophth. **7**:89, 1924.

life and rarely is seen in adults. Maxwell [11] reported a case occurring in a fetus at term. Our youngest patient was 6 weeks old; our oldest, 66 years. Figure 1 gives the incidence at each age by five year periods. While no period of life is exempt, 166 patients, or 81.8 per cent, were either under 5 or between 15 and 30 years of age. Of 64 patients below the age of 5, 30 were less than 1 year old, and of these 22 were less than 6 months of age. This confirms the opinion of others that the disease is one of early life. The increased incidence in the second and third decades can be explained by the number of soldiers and apprentices seen with the disease. These persons, who are usually between the ages of 15 and 30, are underpaid and poorly fed, and they are given long, hard hours of work. They constituted approximately

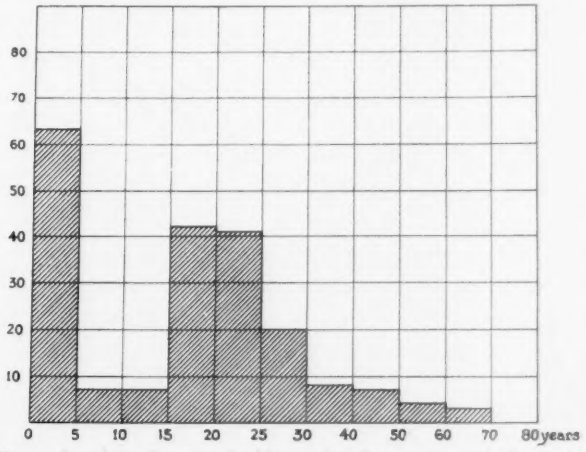

Fig. 1.—Chart showing the age incidence by five year periods in 203 cases of avitaminosis A.

40 per cent of our patients and, together with students, comprised 90 per cent of those in the second and third decades of life.

Sex is probably of no significance in the causation of the disease. Of our series 80 per cent were males; but this probably can be explained by the large number of soldiers and apprentices included in the series. Also, in this clinic the ratio of patients admitted is 58 per cent males to 42 per cent females; so one may expect a larger percentage of males than of females in any series of patients.

Diet is the factor of prime importance in the causation of this deficiency disease as well as of all others. If there is an insufficient utilization of vitamin A by the body, for whatever cause, over a period of time long enough to deplete the body stores of this factor, the disease

11. Maxwell, J. P.: Vitamin Deficiency in the Antenatal Period: Its Effect on Mother and Infant, J. Obst. & Gynaec. Brit. Emp. **39**:764, 1932.

becomes manifest. According to Blegvad,[10] this may be brought about in any of the following ways:

1. By reduced doses of vitamin A.
   A. Food poor in vitamin A.
   B. Deficient absorption of vitamin A (digestive disease).
2. By increased consumption of vitamin A.
   A. During rapid growth.
   B. During a severe disease.

An analysis of our cases confirms these findings. As stated before, the average diet of the Chinese contains subminimal doses of vitamin A. But our patients were below the average in this respect. Of 154 patients whose dietary history is known, 29, or 19 per cent, had a diet totally deficient in vitamin A while 110 others, 71.4 per cent, had diets very poor in this substance. In the diet of the latter group, vitamin A usually was obtained from white cabbage or from bits of meat eaten once or twice a month on festival days and was negligible in amount. As in Blegvad's series, the length of time the patients were able to subsist on these diets before the development of keratomalacia or other symptoms varied inversely with the age of the patient and directly with his nutritional status before taking the diet. In other words, the younger or the more poorly nourished the person, the shorter the time required for the development of deficiency symptoms.

Diseases that might be expected to reduce the absorption of vitamin A from the intestinal tract were present in 33 patients. There were 22 patients with dysentery, 9 with simple, nonspecific infantile diarrhea or enterocolitis and 2 with advanced disease of the liver. These diseases all have been incriminated as factors contributing to the development of avitaminoses by other writers. They were present, and apparently were the chief etiologic agent, in all the 15 patients who were known to have been on adequate diets. They may act not only by preventing absorption but by raising metabolism and causing increased utilization of the vitamin. Other conditions, such as tuberculosis, kala-azar, pneumonia, empyema and syphilis, were frequently the primary disorder in these patients. They may also contribute to the excessive utilization of the vitamins, as suggested by Blegvad, and undoubtedly they cause the onset of deficiency symptoms in many patients who previously have had a "marginal" intake of substances.

The effect of growth is not well demonstrated in this series because there is a high percentage of adults. However, the seasonal incidence of the disease is remarkable. In 177 cases we were able to determine accurately the date of the onset of symptoms (fig. 2). The highest figures were obtained for the months of January, February, March and July. This double yearly peak is of considerable interest. In the winter

fresh green vegetables are scarce in Peiping, and the general population lives chiefly on white cabbage and cereals with very little meat, eggs and dairy products. It is natural, therefore, that avitaminosis should become manifest. In the summer there is an abundance of fresh green vegetables which can be obtained by all. But dysentery and the other diarrheal diseases make their appearance and initiate many cases of avitaminosis. In occidental countries, where dysentery is less severe and less frequent, the disease is unusual except in the winter and spring months, or in artificially fed infants who either are given inadequate diets or are suffering from other chronic illnesses.[12]

PATHOLOGY

Most of the present knowledge of the pathologic anatomy and pathogenesis of avitaminosis A is derived from studies made on experi-

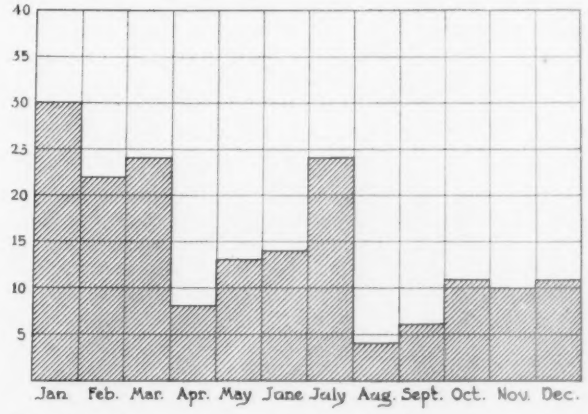

Fig. 2.—Chart showing the seasonal incidence of 177 cases of avitaminosis A in Peiping during a thirty year period.

mental animals. The first anatomic studies were made by Goldschmidt [13] and by Freise, Goldschmidt and Frank,[14] who examined histologically the eyes of rats which had been fed diets deficient in vitamin A and which had shown clinical evidence of xerophthalmia or keratomalacia. They found that the earlier changes in the cornea consisted of keratinization of the upper layer of the epithelium. In severe cases the cornea became necrotic, and infiltrated by many leukocytes, and it contained large numbers of bacteria. Similar studies were made by Stephenson

12. Blackfan, K. D., and Wolbach, S. B.: Vitamin A Deficiency in Infants, J. Pediat. **3**:679, 1933.

13. Goldschmidt, M.: Experimenteller Beitrag zur Ätiologie der Keratomalacie, Arch. f. Ophth. **90**:354, 1915.

14. Freise, E.; Goldschmidt, M., and Frank A.: Experimentelle Beiträge zur Ätiologie der Keratomalacia, Monatschr. f. Kinderh. **13**:424, 1915.

and Clark,[15] but they failed to find distinctive pathologic changes in the corneas. The breakdown of the corneal tissue was considered by them to be due to bacterial invasion. Later studies were made by Cramer, Drew and Mottram [16] and by Meyerstein,[17] and they also failed to find any characteristic changes in the cornea. Davis and Outhouse [18] and Wason [19] studied also the other organs of the body; they likewise obtained negative results.

The first thorough study of the pathologic anatomy of avitaminosis A was made by Mori [20] in 1922. He found that the earlier lesions in the eyes of rats fed diets deficient in vitamin A consisted of cornification of the outer layer of epithelial cells of the bulbar conjunctiva and formation of keratohyaline granules in the cells of the second layer of the mucosal epithelium. In advanced cases the mucosal epithelium became necrotic and ulcerated. The author stated the belief that the xerotic changes of the epithelium are the essential features in vitamin A deficiency and are due to the dryness of the tissue and that ulceration and perforation of the cornea are due to secondary bacterial infection.

In another paper Mori [21] recorded pathologic changes in the paraocular glands as well as other organs of the body. The lacrimal glands were markedly atrophic; their epithelial cells were shrunken and showed no secretory activity. The epithelium of the ducts of the meibomian glands showed very marked xerotic changes resulting in the occlusion of the lumen of the duct and cystic dilatation of the glands. The author concluded that the dryness and xerotic changes in the cornea and in the conjunctiva were due to lack or diminution of secretion of these glands.

In the salivary glands he found little or no secretory activity. The main ducts were often found to be occluded by the desquamated keratinized epithelium. The epithelium of the trachea and larynx also

15. Stephenson, M., and Clark, A. B.: A Contribution to the Study of Keratomalacia Among Rats, Biochem. J. **14**:502, 1920.

16. Cramer, W.; Drew, A. H., and Mottram, J. C.: On the Function of the Lymphocytes and of Lymphoid Tissue in Nutrition, with Special Reference to the Vitamin Problem, Lancet **2**:1202, 1921.

17. Meyerstein, A.: Anatomische Untersuchungen zur Frage der akzessorischen Nährstoffe, Virchows Arch. f. path. Anat. **239**:350, 1922.

18. Davis, M., and Outhouse, J.: Effect of a Ration Low in Fat Soluble "A" on the Tissues of Rats, Am. J. Dis. Child. **21**:307 (March) 1921.

19. Wason, I. M.: Ophthalmia Associated with A Dietary Deficiency in Fat Soluble Vitamin (A): A Study of the Pathology, J. A. M. A. **76**:908 (April 2) 1921.

20. Mori, S.: Primary Changes in Eyes of Rats which Result from Deficiency of Fat-Soluble A in Diet, J. A. M. A. **79**:197 (July 15) 1922.

21. Mori, S.: The Changes in the Para-Ocular Glands Which Follow the Administration of Diets Low in Fat Soluble A, with Notes of the Effect of the Same Diets on the Salivary Glands and the Mucosa of the Larynx and Trachea, Bull. Johns Hopkins Hosp. **33**:357, 1922.

showed marked metaplastic changes which first occurred in the larynx and then in the trachea and bronchi. He studied other organs of the body, including the liver, pancreas, intestines, kidneys and thyroid, but found no remarkable changes.

Much of the present knowledge of the pathology and the pathogenesis of avitaminosis A is the result of the work of Wolbach and Howe.[22] They demonstrated definitely that the specific changes in the tissues in vitamin A deficiency affect primarily the epithelial tissues. The changes consist of substitution of keratinized stratified squamous epithelium for normal columnar or nonkeratinized stratified squamous epithelium. Such changes were observed in various parts of the genito-urinary tract, the respiratory tract and the alimentary tract and in the eyes and paraocular glands; they were considered by the authors just mentioned to be due not to infection or decreased secretion but to deprivation of vitamin A. Other changes consisted of atrophy of glandular organs, emaciation and localized edema of the testes and of the salivary glands. The findings of Wolbach and Howe later were confirmed amply by Goldblatt and Benischek,[23] Tyson and Smith,[24] Thatcher and Sure [25] and many others.

The central nervous system in animals fed diets deficient in vitamin A was studied by a number of authors. Mellanby,[26] using Marchi's staining method, described demyelinization of nerve fibers of the spinal cords of puppies fed diets containing large amounts of cereal but deficient in vitamin A or carotene. His work was confirmed by Zimmerman.[27] But Grinker and Kandel,[28] Weil [29] and Davison [30] were unable to find significant changes in the central nervous system of monkeys and rats fed on deficient diets.

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22. Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat-Soluble A Vitamin, J. Exper. Med. **42**:753, 1925; Epithelial Repair in Recovery from Vitamin A Deficiency. An Experimental Study, ibid. **57**:511, 1933.

23. Goldblatt, H., and Benischek, M.: Vitamin A Deficiency and Metaplasia, J. Exper. Med. **46**:699, 1927.

24. Tyson, M. D., and Smith, A. H.: Tissue Changes Associated with Vitamin A Deficiency in the Rat, Am. J. Path. **5**:57, 1929.

25. Thatcher, H. S., and Sure, B.: Avitaminosis: Pathologic Changes in Tissues of the Albino Rat During Early Stages of Vitamin A Deficiency, Arch. Path. **13**:756, 1932.

26. Mellanby, E.: The Experimental Production and Prevention of Degeneration in the Spinal Cord, Brain **54**:247, 1931.

27. Zimmerman, H. M.: Lesions of the Nervous System in Vitamin Deficiency: I. Rats on a Diet Low in Vitamin A, J. Exper. Med. **57**:215, 1933.

28. Grinker, R. R., and Kandel, E.: Experimental Vitamin (A, B, B_2 and B Complex) Deficiency: Histologic Changes in the Central Nervous System, Arch. Neurol & Psychiat. **30**:1287 (Dec.) 1933.

29. Weil, A., in discussion on Grinker and Kandel.[28]

30. Davison, C., in discussion on Grinker and Kandel.[28]

Sterility is a constant finding in rats fed diets deficient in vitamin A. Evans [31] found that male rats maintained on diets adequate in vitamin E but low in vitamin A became sterile by the third month of life, while those maintained on diets totally deficient in vitamin E but with ample supply of vitamin A did not become sterile until much later. Examination of the testes showed marked degenerative changes of the organ in the absence of vitamin A. Wolbach stated the belief that the metaplastic changes in the uterine mucosa may play an important rôle in the causation of sterility among these animals.

Very few thorough pathologic studies of avitaminosis A in human beings have been reported in the literature. The first detailed description of the pathologic anatomy was made by Leber [32] in 1883 in the course of his study of a group of cases of xerosis of the conjunctiva and keratomalacia in infants, when the etiology of these conditions was still not clear. Leber found hyperplasia of corneoconjunctival mucosa, with marked flattening of the superficial epithelium, which was hard and had a pearly appearance. He observed, and gave a good illustration of, marked metaplasia and keratinization of the mucosa of the renal pelvis, which he considered as of the same nature as the change of the cornea and conjunctiva. The next complete description of a fatal case of avitaminosis A was reported forty years later, in 1923, by Wilson and DuBois.[33] They found keratinizing metaplasia in the lungs, the uterus and the pancreatic ducts. These changes are considered by Wolbach and Howe to be identical with lesions found in experimental rats.

A third case was presented by Thatcher and Sure [25] in 1932. They found occasional metaplasia in the cells of the ducts of sublingual and of submaxillary glands and in epithelial cells of the tracheal mucosa.

In their study of 13 cases of avitaminosis A in infants Blackfan and Wolbach [12] recorded autopsy observations in 11, including a case previously reported by Wilson and DuBois. In 7 of the 13 cases there was no clinical evidence of this condition; the diagnosis of avitaminosis A was made only by the observation of characteristic epithelial changes in one or more organs.

Dryness and scaliness of the skin in avitaminosis A were described by many authors, but Frazier and Hu [34] were the first to associate a

31. Evans, H. M.: Testicular Degeneration Due to Inadequate Vitamin A in Cases Where E is Adequate, Am. J. Physiol. **99**:477, 1932.

32. Leber, T.: Über die Xerosis der Bindehaut und die infantile Hornhautverschwärung, Arch. f. Ophth. **29**:225, 1883.

33. Wilson, J. R., and DuBois, R. O.: Report of a Fatal Case of Keratomalacia in an Infant, with Postmortem Examination, Am. J. Dis. Child. **26**:431 (Nov.) 1923.

34. Frazier, C. N., and Hu, C.: Cutaneous Lesions Associated with a Deficiency in Vitamin A in Man, Arch. Int. Med. **48**:507 (Sept.) 1931.

peculiar papular lesion with this disease. Loewenthal [35] recently observed 130 cases of this peculiar dermatosis among prisoners in Africa who presumably had received deficient diets. Microscopically the lesions consisted of small or large papules arising from the pilosebaceous follicles. The openings of these follicles were plugged up by masses of cornified epithelium. The adjacent epidermis showed marked hyperplasia, and the interpapillary processes were greatly enlarged. The cutis vera around these follicles showed a chronic inflammatory reaction. There was also marked atrophy of the sebaceous and the sweat glands.

In our autopsies we found that the lesions of the eye were the most frequent, occurring in 16 of 17 cases. They started in the form of keratinization of the cornea and conjunctiva with disappearance of mucous cells. The epithelium of the cornea was hyperplastic and

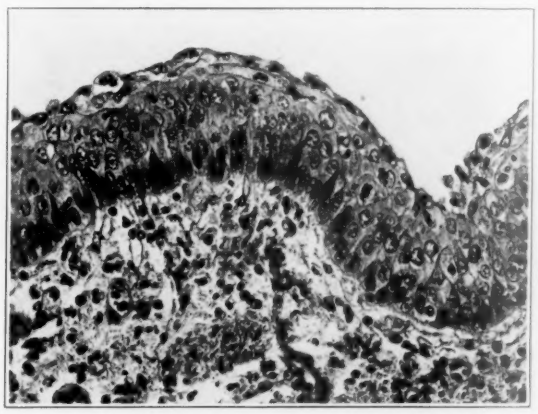

Fig. 3 (case 14).—Metaplasia of the lining epithelium of the trachea (× 230).

thickened. The corneal stroma showed first edema and then necrosis. This was followed eventually by ulceration and secondary bacterial infection. The tunica propria of the cornea was thickened and infiltrated by lymphoid cells and leukocytes. Newly formed blood vessels grew from the limbus toward the center of the cornea. Perforation of the corneal ulcer was frequently found, and in a few cases it led to panophthalmitis. When treatment was given before perforation took place, the ulceration sometimes healed, but there was always a permanent scar.

Changes in the respiratory tract ranked next in frequency. Epithelial metaplasia was present in larynx or trachea [36] in 8 of our 17 cases. The changes consisted of atrophy and replacement of the original columnar ciliated epithelium by stratified squamous epithelium, which in some cases

35. Loewenthal, L. J. A.: A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch. Dermat. & Syph. **28**:700 (Nov.) 1933.

36. There were no specimens from the nose and nasopharynx available for study.

showed superficial keratinization. In more severe cases the epithelial changes sometimes extended even to the smaller branches of the bronchi. Associated with these epithelial changes there was usually an infiltration of the subepithelial tissue by many lymphoid cells, mononuclear wandering cells and varying numbers of leukocytes. The inflammatory reaction was as a rule more marked around the mucous glands, some of which were dilated. The dilatation of these glands seems to have been due to obstruction of the ducts of the glands as a result of similar metaplastic changes of the ductal mucosa.

In the digestive tract the esophagus was the only organ in which epithelial changes occurred. Of our 17 cases definite keratinization of the esophageal mucosa was present in 5. In some cases the keratinization

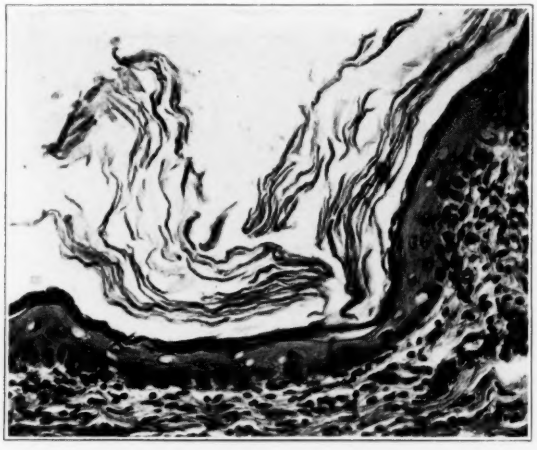

Fig. 4 (case 14).—Marked keratinization of the esophageal mucosa (× 230).

was so marked that the mucosa closely resembled hyperkeratotic epidermis. The epithelium of the ducts of the esophageal glands was hyperplastic, causing partial or almost complete obstruction. The submucosa usually was infiltrated by a moderate number of lymphoid cells and a few mononuclear wandering cells. In the pancreas, metaplastic changes were seen only in the small ducts in 1 case.

Changes in the urinary system were found in 3 of our 17 cases and consisted of slight or early metaplastic changes in the epithelium of the renal pelvis. The ureter and bladder showed no noticeable alteration in the mucosa. Of the genital organs epithelial metaplasia was found in the prostate of only 1 of the 10 males and in the uterine mucosa of only 1 of the 7 females.

The lesions of the skin in some of the cases were very striking. They consisted of many large or small and more or less horny papules in the pilosebaceous follicles. Microscopically these follicles were found

to be markedly distended with concentric layers of keratinized epithelium. The sebaceous glands were extremely atrophic, and in many areas they seemed to have disappeared completely. The sweat glands were very few in number and also showed marked atrophy. The

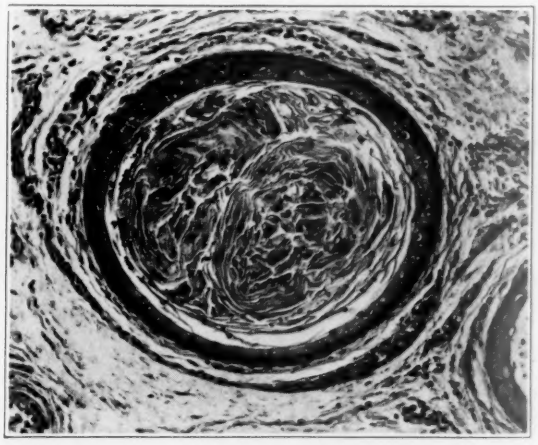

Fig. 5 (case 8).—Keratinization and complete occlusion of the duct of an esophageal gland (× 120).

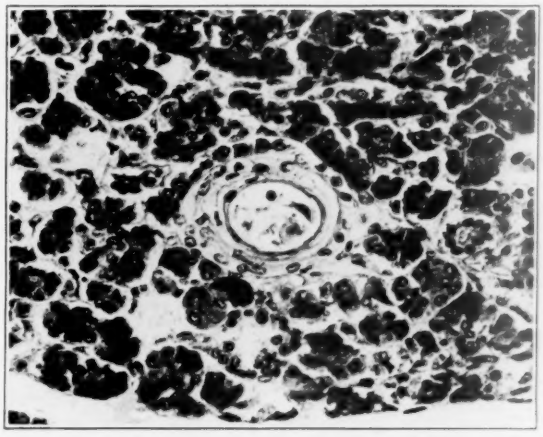

Fig. 6 (case 4).—Epithelial metaplasia with partial occlusion of a small pancreatic duct (× 230).

epidermis around the pilosebaceous follicles was very thick and hyperplastic. There was also considerable chronic inflammatory reaction in the cutis vera, especially around the papular lesions.

Hemosiderosis of the liver and spleen, as described by Blackfan and Wolbach,[13] was present in about 50 per cent of our patients who came

to autopsy. As this condition occurs frequently in a great variety of diseases, it seems probable that hemosiderosis is not directly related to avitaminosis A.

Degeneration and hyalinization of the epithelium of the seminiferous tubules as observed by Evans [31] in experimental animals was present

Fig. 7 (case 14).—Metaplasia and hyperplasia of the glandular epithelium of the prostatic gland (× 230).

Fig. 8 (case 14).—Metaplasia with partial keratinization of the epithelium of the main duct of the prostatic gland (× 230).

in 2 adults; 1 of these patients died of chronic pulmonary tuberculosis and the other of chronic dysentery. It is difficult to attribute these changes to avitaminosis A, since they are frequently present after death from chronic infectious or wasting diseases.

Among the patients who came to necropsy there were 3 with definite rickets. The significance of the presence of rickets in these patients will be discussed later.

SYMPTOMATOLOGY

The symptoms of keratomalacia have been described fully by Pillat,[37] Hsu,[38] Wright,[39] Blegvad,[10] Bloch,[8] Blackfan and Wolbach [12] and others, and a complete discussion of them here is unnecessary. However, a résumé of the chief complaints with an attempt to correlate the pathologic observations is in order.

Fig. 9 (case 2).—The lower extremities of an infant with keratomalacia, showing advanced active rickets.

The ocular symptoms are perhaps the most striking. In adults and older children, hemeralopia or night blindness is frequently the earliest complaint. This was present in 50 of our patients. It is insidious in onset and may be present for weeks or even months before the onset of other symptoms. It has been demonstrated in rats on a diet deficient in

37 (*a*) Pillat, A.: Does Keratomalacia Exist in Adults? Arch. Ophth. **2**:256 (Sept.) and 399 (Oct.) 1929; (*b*) The General Symptoms of Keratomalacia of Adults, China M. J. **43**:907, 1929; (*c*) Main Symptoms of the Eye in Vitamin A Deficiency in Adults, Nat. M. J. China **15**:614, 1929.

38. Hsu, K. L.: Nutritional Keratomalacia, China M. J. **41**:825, 1927.

39. Wright, R. E.: Keratomalacia in Southern India, Brit. J. Ophth. **6**:164, 1922.

vitamin A by Holm,[40] and it has been found in these animals to be due to a delay in the regeneration of visual purple (Fridericia and Holm[41]). We were unable to study this process in patients who came to autopsy. The low incidence of this complaint does not mean that the other patients were free from the pathologic processes involved. Chou[42] found a reduced power of adaptation to dark in 13 of 20 patients with very early ocular signs of vitamin A deficiency. Of these, only 4 had subjective complaints of night blindness, and in them the power of adaptation to dark was reduced to less than 50 per cent of the normal. It is probable that a failure of adaptation to dark is present in almost all patients with the disease before the condition is well established.

If this symptom is missed, however, there are few or no warning signals in the eyes until the evidence of involvement becomes grossly apparent. At that time, the patient complains of pain, lacrimation, redness of the eyes and photophobia. These symptoms usually occur almost simultaneously and are of sudden onset. The typical story is that the patient suddenly feels a pain as if he had a grain of sand in his eye. Following this the eye becomes inflamed, lacrimation becomes profuse and photophobia develops. These symptoms were concomitantly present in about 50 per cent of our patients; there was a much higher percentage in the older children and in the adults who were able to complain of subjective symptoms. As the disease advances, a conjunctival discharge is very apt to develop, so that the patient complains that his eyelids are glued together in the morning. Still later, though the interval may be extremely short in young patients or in those on a totally deficient diet, failure of vision, usually associated with a spreading white spot on the cornea, becomes manifest. This may progress slowly or may extend to complete blindness in a few hours or days. Rarely, swelling of the eyelids, blepharospasm, itching or dryness of the eyes may be complained of.

These early symptoms develop when the metaplastic changes in the conjunctiva become so severe as to interfere with the normal secretion of the mucous cells. The dryness and pain can be accounted for by the thickening and wrinkling of the conjunctiva in these patients. Secondary infection, which takes place early, can explain the redness and the dis-

40. Holm, E.: Demonstration of Hemeralopia in Rats Nourished on Food Devoid of Fat-Soluble A Vitamin, Am. J. Physiol. **73**:79, 1925.

41. Fridericia, L. S., and Holm, E.: Experimental Contribution to Study of Relation Between Night Blindness and Malnutrition: Influence of Deficiency of Fat-Soluble A-Vitamin Diet on Visual Purple in the Eyes of Rats, Am. J. Physiol. **73**:63, 1925.

42. Chou, C. H.: Effect of Vitamin Deficiency on Light Sense in Cases of Xerosis and Pigmentation of the Conjunctiva, Nat. M. J. China **16**:365, 1930.

charge, and the whole foreign body reaction may cause the increased lacrimation which is usually excessive.

The sequence of involvement of the eyes is of some interest. It was stated reliably in 173 cases in this series. Of these, one eye alone was involved in 14, or 8 per cent, while in 41, or 23.7 per cent, one eye was involved well in advance of the other. In the remaining patients the involvement was described as being simultaneous or almost so. In the cases in which one eye was involved before the other, the right and the left eye were about equally attacked.

The general symptoms of avitaminosis A follow a much less clearcut pattern. As has been emphasized by Bloch,[8] Blackfan and Wolbach [13] and others, well nourished persons who adopt a diet deficient in vitamin A show loss of weight as the initial symptom. In our patients, however, there were so many already poorly nourished persons that loss of weight was a subjective symptom in only 10 per cent of the cases. Better observation might have increased this number, but, as will be seen later, there were a fairly large number who at the time of admission were well nourished. Loss of appetite was about as common as loss of weight and usually was associated with it.

More constant general symptoms were diarrhea, fever and cough. In many instances diarrhea could be accounted for on the basis of primary dysentery or some other nutritional disturbance. However, it was present in roughly twice as many cases as we were able to assign to the category of primary diarrheal diseases. Moreover, as pointed out by Pillat,[43] it is frequently secondary to other evidence of avitaminosis A and is relieved by a diet high in fat and in vitamins, a treatment which usually makes primary diarrheal disorders more severe. We are unable to explain this symptom by our pathologic observations. Atrophy of the tips of the intestinal villi and of the mucus-secreting cells of the intestinal mucosa has been described in animals.[44] We were unable to confirm these findings in our material. The atrophy of the mucous cells seems unlikely, however, in view of the large amounts of mucus secreted by patients with avitaminosis A complicating, or complicated by, dysentery. Constipation was a rare complaint. Fever and cough each were present in about 25 per cent of our series. They, too, were at times explainable on the basis of complicating disorders but were seen frequently in patients with otherwise uncomplicated avitaminosis A. The cough may be due to dryness and irritation of the trachea from loss of mucous secretion and from change of the ciliated epithelium to a keratinizing variety. Rarely is the cough productive, sputum being recorded in only 11 of our cases. The explanation of the fever is much

43. Pillat.[37a, b]

44. Cramer, W.: On the Mode of Action of Vitamins, Lancet **1**:1046, 1923.

less simple. It usually lasted until the ocular symptoms began to improve and then subsided.[37b] Several authors have attempted to ascribe it to collapse of the peripheral heat-regulating mechanism of the body, particularly to decreased perspiration. We were unable to prove that this is not the case, but it seems unlikely. Histologic changes in the sweat glands are late manifestations of avitaminosis A, and fever is present much more frequently than are anatomic changes in the glands. Also, the fever subsides in a very few days after administration of vitamin A, whereas the cutaneous lesions are among the last to disappear. It seems likely that the fever is due either to absorption of toxins through the altered epithelium or to metabolic changes attempting a more rapid utilization of fat by the body.

There were several other symptoms less frequently encountered but definitely associated with avitaminosis A, such as headache, hoarseness of the voice, vomiting and general weakness. Headache was a late symptom, coming with advanced ocular disease. Usually it was frontal and unilateral, on the side of the involved eye. If both eyes were equally involved, the headache was sometimes bilateral. It was usually sharp, piercing and difficult to control. Hoarseness was not very frequent but occasionally was seen in late cases. It probably resulted from epithelial changes in the larynx. Vomiting was infrequently present, but was at times very bothersome. Unexplained convulsions occurred in 4 of our patients. In one instance (case 11) they began in the sixth week of life in an infant whose mother apparently had suffered from lack of vitamin A during her pregnancy. No specific lesions were found to explain the convulsions in any of the cases.

Foul breath was complained of in a few instances. It was usually associated with atrophic rhinitis. The relation of this condition to avitaminosis A has not been studied carefully. Cutaneous symptoms of all types were most notable by their infrequency. This was particularly true of sepsis of the skin which was seen little in this series of patients, if any more frequently than in any other series. Other general symptoms, such as edema, pain in the chest or the abdomen, otorrhea, rhinorrhea, hemoptysis, dyspnea and cyanosis, were rarely seen, and then only as the result of complicating disease.

EXAMINATION

The findings on general physical examination may be characteristic in this condition. There are not as yet satisfactory standards for normal nutritional and developmental status in the Chinese, and hence evaluation of these qualities in any person is difficult. However, as well as can be judged, they seem to be altered in the presence of avitaminosis A. It was estimated that 20 or more of all the patients examined suffered from underdevelopment. This was most marked in the younger patients.

It presumably is due to lack of vitamin A, though it may be due to associated deficiencies. It does, however, indicate prolonged lack of structural foods. The nutritional status is usually below normal, 71 per cent of the patients being classified as "poorly nourished." Of these 34 per cent were suffering from severe grades of undernutrition or emaciation. That absence of stored fat is not essential to the development of vitamin A deficiency, however, is obvious from the fact that 41 patients, 29 per cent of those whose nutritional status was recorded, were said to be well nourished. Pillat [37b] said that in early cases the patient is apt to be quite pudgy in appearance.

The skin presents a variety of abnormalities that are more or less characteristic of avitaminosis A. The most frequent, but the least characteristic, of these is dryness. This is present in about a quarter of all the patients and has been ascribed by Pillat and others to a deficient function of the sebaceous and sweat glands. Pillat also described a "peculiar pale gray color of the skin which in advanced cases takes a yellowish hue." The condition is most marked about the temples, on the forearms and over the upper part of the chest. It has been ascribed to an increase in the pigment of the basal cell layer of the epidermis, a change similar to that producing the characteristic pigmentation of the eye. The presence of numerous comedones on the face has been observed frequently. These disappear spontaneously when proper treatment is instituted.

The most specific cutaneous lesions seen were those described first by Frazier and Hu [34] and later by Loewenthal.[35] These lesions vary from a slight roughening to an extreme involvement of the whole skin with papular, cornified lesions surrounding the hair follicles (fig. 10). These follicular keratotic lesions are most marked over the extensor surfaces of the extremities and over the shoulders. They are seen most often in adults, rarely in children. Frequently they are present before the ocular symptoms of avitaminosis begin and under the treatment they subside much more slowly. In association with these lesions there is usually an ashen gray color or an excess pigmentation of the skin, as described before.

Much less frequently there are atrophic cutaneous ulcers which heal promptly with dietary therapy but which are extremely persistent under all other forms of treatment. These have not been studied histologically, but they are found only in cases of avitaminosis A of long standing, and they are thought by Pillat to be specific lesions of the disease.

The hair and nails are involved in a few late cases. The hair becomes dry, coarse and brittle, and it frequently falls out. The nails in a few cases (Pillat [43]) are found to be transversely or longitudinally furrowed, lusterless and evidently abnormal. These conditions are said to improve remarkably under specific treatment with vitamin A.

The question of sepsis of the skin in vitamin A deficiency has been argued frequently. Frazier and Hu [34] noted sepsis frequently as a late phenomenon in the patients with other cutaneous manifestations studied by them. Loewenthal [35] was impressed by its infrequency in his patients who had frequent baths. In our total series of patients, sepsis of the skin was found very rarely. Impetigo and cutaneous ulcers were described in less than 5 per cent of the cases, a very low incidence considering the low economic state and poor hygienic surroundings of our patients. It has been fairly well established by Wright [45] and his associates, by Hess [46] and by Hess, Lewis and Barenberg [47] that excess

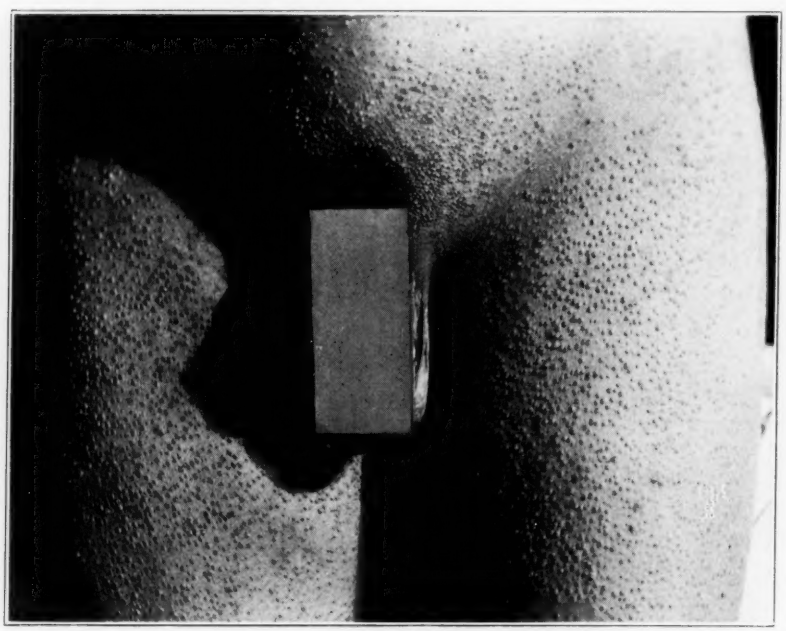

Fig. 10.—Papular hyperkeratotic cutaneous lesions associated with avitaminosis A in a youth 17 years old. Three months after the appearance of these lesions night blindness and keratomalacia developed (courtesy of Dr. C. N. Frazier).

vitamin A in the diet has no protective action against acute respiratory infections. We feel that the same is true with regard to sepsis of the skin. While sepsis may occur frequently as a late complication, it rarely initiates the symptoms or pathologic findings in the skin of patients with avitaminosis A.

45. Wright, H. P.; Frost, J. B.; Puchel, F., and Lawrence, M. R.: Vitamin "A" and the Common Cold, Canad. M. A. J. **25**:65, 1931.

46. Hess, A. F.: Diet, Nutrition and Infection, New England J. Med. **207**: 637, 1932.

47. Hess, A. F.; Lewis, J. M., and Barenberg, L. H.: Does Our Dietary Require Vitamin A Supplement? J. A. M. A. **101**:657 (Aug. 26) 1933.

Pyrexia is found in this condition. Frequently it is caused by pyogenic or other complicating agents, but it is not usually present in uncomplicated xerophthalmia or keratomalacia. The explanation for this is not certain, but under specific treatment the fever leaves in from four to seven days, the usual period in which improvement is noted in the condition of the eye.

Enlargement of the spleen and liver was found more frequently in this series of patients than should be expected from chance and associated diseases. The spleen was palpable in 37 cases and the liver enlarged in 18 cases. We have no explanation to offer for this. The only change noted in some of these organs at autopsy was hemosiderosis. In several cases there was excessive storage of fat in the liver.

Atrophic rhinitis was present in 6 cases. These were of long duration, and the patients were seen late in the period covered by our study. From animal experiments, it is to be expected that there will be changes in the nasal mucous membrane. Such changes were found by Blackfan and Wolbach [12] in 1 of their cases. We have been able to demonstrate cornified epithelial cells in scrapings from the nose in 14 of 17 cases of avitaminosis A. It is probable, therefore, that there is an etiologic relationship between avitaminosis and atrophy of the nasal mucosa, but at present conclusive evidence for this is lacking. Further studies with histologic examinations by biopsy and prolonged follow-up of these patients is highly desirable.

Toxemia, prostration, dehydration, edema, petechial rash and other such frequent symptoms are dependent on the associated pathologic state and apparently are not primarily due to the avitaminoses per se. They are entirely too numerous to be discussed in detail.

The ocular findings are much more specific. They have been carefully studied by Pillat [48] and others and will be given the briefest consideration. The extent of involvement varies directly with the severity and duration of the disease. Redness and injection of the conjunctiva are the most frequent findings and are present in almost all cases. In the very earliest cases there is loss of luster of the conjunctiva, which dries quickly and easily on exposure. As the disease progresses definite xerosis of the conjunctiva appears. Bitot's spots become evident, and later there is wrinkling of the conjunctiva with a dry leathery or greasy appearance of the whole structure. With these advancing signs in the conjunctiva, the cornea also becomes involved, first showing only a mild loss of luster and reduced sensibility (John [49]). Scrapings from the eyeball at this stage show Bacillus xerosis in the degenerated

48. Pillat.[37a, c]

49. John, I.: The Disturbances of Sensibility of the Cornea and Conjunctiva in Xerosis and Keratomalacia of Adults, Arch. Ophth. **5**:374 (March) 1931.

epithelial cells. Later there is a real xerosis or dryness of the cornea which is quickly followed by the development of infiltrates or ulcers, the typical picture of keratomalacia. In even later stages the whole cornea of one or both eyes may be sloughed off.

Pigmentation of the conjunctiva is seen in a very high percentage of the cases in China. It is rare in children but is present in almost all adults. This has been studied carefully by Mori [50] and Pillat,[51] who have found it to be due to: (1) dendritic cells or melanoblasts which are situated in the basal epithelial layers and send their filamentous projections into the intercellular spaces and (2) pigment caps produced on the distal poles of the nuclei of the normal cells. This pigment is most marked in the region of the semilunar fold and caruncle and extends into the lower fornix and over the bulbar and palpebral conjunctiva. It has been described by almost all authors who deal with patients of the Oriental races but has not been reported as occurring in European patients.

Swelling of the lids with purulent blepharitis and conjunctivitis is an uncommon finding.

Laboratory studies yielded variable results in these cases. Blood counts and hemoglobin estimations were made in 176 cases. Of these 78 were apparently uncomplicated cases of avitaminosis A, while in 98 the condition was complicated by pyogenic, protozoal or other definite deficiency diseases. In the uncomplicated cases there was little evidence of secondary anemia, the average hemoglobin content being 86 per cent (Sahli) and the average erythrocyte count 4,640,000 per cubic millimeter of blood. Furthermore, in only 38 per cent of the uncomplicated cases was the hemoglobin content below 85 per cent or the erythrocyte count below 4,500,000. In the complicated cases, however, the average findings were hemoglobin, 72 per cent, and erythrocytes, 3,700,000; there were 80 per cent with hemoglobin estimations below 85 per cent, and 65 per cent of the patients with erythrocyte counts below 4,500,000. When one considers that all these patients probably had other deficiencies besides that of vitamin A, one sees that this deficiency has no tendency per se to produce anemia, though it may affect the hematopoietic system so as to make the development of anemia as a result of other agents or deficiencies much easier. This point should be investigated further. The leukocytes of the blood show no characteristic response to avitaminosis A but reflect the usual picture of whatever complicating disease may be present.

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50. Mori, S.: Pathology of the Pigmentation of the Bulbar Conjunctiva in Xerosis Epithelialis Conjunctivae, J. Orient. Med. **2**:103, 1924.

51. Pillat, A.: Production of Pigment in the Conjunctiva in Night Blindness, Prexerosis, Xerosis and Keratomalacia of Adults, Arch. Ophth. **9**:25 (Jan.) 1933.

The chemistry of the blood serum frequently shows changes indicating deficiencies other than that of vitamin A. The serum proteins were determined in 25 cases. In 19 cases determinations were made of the albumin and globulin fractions. The greatest change was noted in the albumin fraction, which was below normal in every instance. It was found to average 2.41 Gm. per hundred cubic centimeters. The lowest value was 1.07 Gm., and the highest was only 3.76 Gm. Of 19 instances in which the determination was made the serum albumin was below 3 Gm. in 14. The globulin fraction showed more marked variations. It ranged from 1.6 to 4.74 Gm. and averaged 2.65 Gm. In 6 it was 2 and in 4 above 3.5 Gm.

The results of the determinations for calcium and for phosphorus were equally variable. These were made in 31 cases, in 10 of which the serologic findings of rickets were noted; i. e., the product of the calcium and the inorganic phosphorus content expressed in milligrams per hundred cubic centimeters of blood serum was less than 30.[52] The calcium content was below 9 mg. per cent in 8 cases, the lowest value being 5.7 mg. per cent. The phosphorus was below 3.5 in 7 cases, the lowest being 2.2 mg. per cent.

Urinalysis also gave inconstant results. In 125 of our cases one or more urinalyses gave completely negative results. Albumin and pus cells were found in 35 and 40 cases, respectively. In many instances they were not more abundant than might be expected in patients equally ill from other causes. Epithelial cells were found in 28 instances, but they were abundant in only 2. Red blood cells and casts were rarely present. Of 13 cases in which we carefully examined fresh specimens of urine there was an abnormal number of squamous epithelial cells in the urine in only 1. In the other cases they were very rare or were absent in uncentrifugated specimens and were few in number in the urinary sediment. This is contrary to the results reported by Spence,[53] Herbert [54] and others, but it conforms to the clinical findings of Blackfan and Wolbach.[12] Also, the clinical finding of clear urine conforms with the slight epithelial metaplasia observed in the urinary tracts of our patients.

COMPLICATIONS

The diseases coexisting with avitaminosis A when the patient was seen can be divided into three categories: (*a*) primary or predisposing

52. Howland, J., and Kramer, B.: Factors Concerned with the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922.

53. Spence, J. C.: Clinical Study of Nutritional Xerophthalmia and Night Blindness, Arch. Dis. Childhood **6**:17, 1931.

54. Herbert, H., in discussion on Mayou, M. S.: Pathological Anatomy of Epithelial Xerosis, Tr. Ophth. Soc. U. Kingdom **24**:9, 1904; in discussion on Collins, E. T.: The Harderian Gland; Xerophthalmia; Vitamin A Deficiency; Keratomalacia, ibid. **50**:201, 1930.

disorders; (*b*) associated or correlative disorders and (*c*) secondary complications. The first group has been considered. It consists of dysentery, infantile diarrhea, enterocolitis, tuberculosis, kala-azar and other usually prolonged illnesses which present the absorption of vitamin A or increase the demand for it or do both. In the second group of correlative diseases one finds chiefly associated dietary deficiencies.[55] Of these, the most frequent was rickets. It was present in 28 instances, in 20 of which there was either roentgenologic or serologic evidence in support of the clinical findings. Rickets was found to be present in 3 patients who came to necropsy. This incidence, 42.5 per cent in patients below 5 years of age, is very high. It is an important finding in that it indicates either that the manifestations of avitaminosis A are so rapid in their onset that the lesions of rickets are unable to heal in the period before death or that osseous growth continues in spite of lack of vitamin A. There is evidence in these cases that both mechanisms may be at work. The associated action of the 2 vitamins would bear further investigation.

Nutritional edema was found in 11 of our cases and, as already stated, the blood serum albumin was low in every case in which fractional determinations were made. The edema disappeared rapidly under dietary treatment in patients who responded favorably. Beriberi was present in a single instance in the series, but this disease is uncommon in North China. There is nothing to prevent its coincident development with avitaminosis A.

The secondary or complicating diseases are usually acute infections. In many instances the disease was well developed at the time of the patient's admission to the hospital, and from the history it often was impossible to determine whether the manifestations of the pyogenic infection or those of the deficiency disease were primary. Therefore, it is possible that some of these conditions may belong in the first group discussed. Nevertheless they were seen sufficiently often as definite secondary diseases to justify their classification in that category. These diseases are chiefly in the nature of respiratory infections. In 6 cases there was acute infection of the upper respiratory tract, while in 9 bronchitis was present, in 21 bronchopneumonia, in 11 otitis media, in 13 sinusitis and in 2 septicemia. As stressed by Blackfan and Wolbach,[12] the pneumonia associated with avitaminosis A is usually a peribronchial interstitial infiltration. It is probable that all these diseases owe their genesis to lowered resistance to organisms due to metaplastic changes in the epithelium lining the organs. Sepsis of the skin was strikingly infrequent in these cases, cutaneous ulcers being present in only 5 and

55. Weech, A. A.: Association of Keratomalacia with Other Deficiency Diseases, Am. J. Dis. Child. **39**: 1153 (June) 1930.

impetigo in 3. Pyelonephritis caused by dysentery bacillus was present in 1. Symptomatic purpura with a decrease in the number of platelets and hemorrhagic rash was present in 4 patients, while typhoid and typhus fevers and erythema nodosum each were seen once.

The ocular complications are second in importance only to the infections of the respiratory tract. The most important of these is panophthalmia secondary to corneal perforation. As the late stages of keratomalacia regularly produce corneal ulcers with perforation and prolapse of the iris, panophthalmia is apt to occur in any advanced case. In 1 instance (case 7) there was a severe conjunctival diphtheria from which virulent Bacillus diphtheriae were cultivated. The cornea was completely sloughed off, and there was severe panophthalmia. This case gave rise to a definite question in diagnosis, but as diphtheria does not cause necrosis of the cornea it was thought that deficiency of vitamin A was an important factor in the process. Trachoma is so frequently seen among poor Chinese [56] that its presence in most of these cases can hardly be reckoned as a complication.

DIAGNOSIS

In well advanced cases diagnosis causes little or no trouble; in very early cases, however, it is more difficult. In older children and adults, incipient night blindness is the earliest detectable sign. Convenient methods of finding this have been devised by Birch-Hirschfeld [57] and by Jeans and Zentmire.[58] In young infants, however, it is practically impossible to detect loss of adaptation to dark. Consequently other methods must be devised. Blackfan and Wolbach suggested examination of the urine, of tracheal secretions or of scrapings from the nose and eye. In any of these the demonstration of cornified epithelial cells is presumptive evidence of avitaminosis A, especially in chronically ill, debilitated infants. However, as pointed out previously, the finding of abnormal numbers of cornified epithelial cells in the urine of these patients is unusual, and its absence cannot be relied on to exclude the disease. Tracheal secretions are very difficult to secure for examination. One of the earliest changes in the trachea is loss of function of the mucus-secreting cells; consequently tracheal secretions are considerably lessened in these children, and a productive cough is rarely encountered. Also, it is very difficult to secure such secretions uncontaminated by the

56. Pillat, A.: Frequency of Deficiency Diseases of the Eye Due to Lack of Vitamin A in a Military Camp North of Peiping, Nat. M. J. China **15**:585, 1929.

57. Birch-Hirschfeld, A.: Über Nachtblindheit im Kriege, Arch. f. Ophth. **92**:273, 1916.

58. Jeans, P. C., and Zentmire, Z.: A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency, J. A. M. A. **102**:892 (March 24) 1934.

more or less cornified epithelial cells of the normal oral cavity. We have been unable to differentiate by staining between the cells obtained by scraping the buccal mucosa of normal patients and that of patients with advanced keratomalacia. Therefore care must be exercised in interpreting the results of examination of tracheal secretions which are obtained by other methods than direct tracheoscopy. We made nasal scrapings from 17 patients with ocular signs of vitamin A deficiency. Of these, 14 had cornified epithelial cells in the scrapings. We have been unable to determine the relative time relation between the onset of the changes here and that of those in the eye, but we feel that this offers an early confirmatory test for the diagnosis. Mouriquand, Rollet and Chaix [59] suggested the use of the slit lamp as the earliest possible means of diagnosing the ocular condition in infants. However, in this clinic the method has been found to be very difficult, as small infants are unable to hold their eyes still. Therefore, it is the practice here to expose the cornea and conjunctiva for from three to five minutes by retracting the lids. In the very earliest cases there will be a slight haziness or loss of luster of the conjunctiva. Scrapings made by sweeping a small spatula lightly across the conjunctiva at this time will show keratinizing epithelial cells. These may be shown to contain B. xerosis and the pneumococcus when properly stained.[60] We believe that this offers one of the most reliable methods of early diagnosis of avitaminosis A, though the condition is so varied in its manifestations that no one procedure will suffice for all cases.

TREATMENT

The treatment of this condition is along simple lines. The general measures consist in giving vitamin A in adequate dosage. In simple, uncomplicated cases this is sufficient. Vitamin A may be supplied by any known form, from any source. Liver has been recognized since ancient times as a cure for hemeralopia.[1] Milk, butter, eggs, animal fats (except pork fat) and fresh green vegetables constitute the commonest food sources of the vitamin. Artificially it may be given as cod liver oil, 15 cc. or more a day being used. In a few instances we have treated patients successfully with halibut liver oil, giving 30 drops (0.5 cc.) of the commercial preparation per day. Recently Brugsch [61] reported successful treatment for the disease by the use of carotene and of a vitamin A preparation.

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59. Mouriquand, G.; Rollet, J., and Chaix: Précarence et avitaminose A, Paris méd. **1**:419, 1930.

60. Pillat, A.: Bakteriologische Befunde bei Praexerosis Corneae, Arch. f. Ophth. **125**:173, 1930.

61. Brugsch, H.: Erfolgreiche Keratomalaziebehandlung beim Menschen durch Karotin und Vogan, Deutsche med. Wchnschr. **59**:325, 1933.

In later cases there is usually secondary infection of the eyes. In these cases the combination of local antiseptics and hot compresses is used with adequate dosage of vitamin A. When there are other complicating diseases the general treatment must be altered to suit the needs of the patient and the pathologic condition involved. We have the impression that in the presence of diarrheal diseases the more concentrated forms of vitamin A, such as halibut liver oil, are more effective than the less concentrated preparations (case 15). Unfortunately we have not yet had opportunity to subject this clinical impression to scientific investigation. When there is evidence of complete lack of absorption of the vitamin from the gastro-intestinal tract it may be given parenterally. Blegvad [62] in 1923 treated 1 patient in this manner with good results, and Bloch [63] in 1924 reported its use with 5 patients. More recently Koehne and Mendel [64] demonstrated the utilization of vitamin A injected subcutaneously and intraperitoneally into dogs.

COMMENT

The most striking feature of avitaminosis A as we have seen it is the great variability in the pathologic process and in the symptoms of the disease. This is particularly true in the earlier cases. Mackay [65] emphasized the frequency of sepsis of the skin in mild avitaminosis A. We have seen very little of this complaint, as has Loewenthal,[35] who stated that in his patients who were given daily baths of soap and water sepsis of the skin was very uncommon. Blackfan and Wolbach [12] emphasized the early incidence of epithelial metaplasia in many hollow viscera in infants with this condition; they believed changes in the eye to be a late manifestation of this deficiency. However, they were unable to examine the eyes of their patients histologically, and apparently they were comparing the onset of microscopic lesions in the internal viscera with macroscopic clinical changes in the eye. In our series of 17 autopsies we found 6 cases in which the patient died of keratomalacia and its complications without any change in the epithelial lining of any of the other organs. However, we had 1 patient (case 16) with epithelial metaplasia in the respiratory tract without keratomalacia. We are willing to agree that ocular symptoms may not occur until late in the disease,

62. Blegvad, O.: Ugesk. f. laeger **85**:942, 1923; quoted in Subcutaneous Injection of Vitamin A, editorial, Brit. M. J. **1**:122, 1924.

63. Bloch, C. E.: Further Clinical Investigations into the Diseases Arising in Consequence of a Deficiency in the Fat-Soluble A Factor, Am. J. Dis. Child. **28**:658 (Dec.) 1924.

64. Koehne, M., and Mendel, L. B.: Utilization of Fatty Oils Given Parenterally, J. Nutrition **1**:399, 1929.

65. Mackay, H. M. M.: Vitamin A Deficiency in Children, Arch. Dis. Childhood **9**:65, 1934.

but in many cases they cause the earliest and most severe complaints. Moreover, one cannot deny the presence of microscopic changes in the eye in the absence of obvious clinical findings in the eye. The following case offers an excellent illustration of this point.

L. H. P., a youth aged 19, entered the hospital in the ophthalmological service on Nov. 13, 1928. He had a swelling in the sclerocorneal junction for two months. A portion of the swelling was removed, but it recurred and he came to the hospital for treatment. Examination showed a diffuse hyaline degeneration of the conjunctiva with no other pathologic changes. A portion of the degenerated tissue was removed, the wound healed, and the patient was discharged in good condition. On Dec. 27, 1928, he returned to the hospital with typical keratomalacia with corneal perforation and prolapse of the iris. The histologic examination of the material removed from the eye during his first admission showed a very greatly thickened conjunctival epithelium. Although there were many goblet cells present the epithelium was definitely stratified and keratinized, and there was a considerable increase in pigment. The diagnosis of early keratomalacia was made at that time, a month before the patient had either subjective symptoms or obvious physical signs of the disease, but he unfortunately did not return to receive the benefit of treatment until the condition was far advanced.

CASE 1.—P. Y. C., a boy aged 2 months, was admitted to the Peiping Foundling Home on Aug. 20, 1929, and brought to the hospital on the following day. The history was entirely unknown.

Examination.—Clinical examination revealed a well developed, emaciated moribund infant with dry and wrinkled skin. There was pitting edema of both feet and legs. Diminished luster of the bulbar conjunctivae and of the corneas, with a small central ulcer in the right cornea, was observed.

Examination of the blood showed: hemoglobin, 71 per cent (Sahli); red cells, 3,400,000; white cells, 15,300; polymorphonuclear neutrophils, 53 per cent; lymphocytes, 42 per cent; monocytes, 5 per cent; calcium, 9.2 mg. per hundred cubic centimeters, and phosphorus, 3.8 mg. Roentgenograms showed no abnormality in the long bones or in the lungs.

Course.—The patient was given a transfusion of blood, daily subcutaneous infusions of a 5 per cent solution of dextrose and general supportive care. He failed to respond and died two days after admission.

Necropsy.—Extensive confluent lobular pneumonia was present. Metaplastic changes of the epithelium was observed only in a few small areas in the tracheal mucosa. The eyes were not available for histologic study.

CASE 2.—C. T. P., a girl aged 8 months, was brought to the hospital on July 16, 1929, for diarrhea, vomiting and fever. The patient had had from one to two loose stools daily for three months, and she had had very numerous watery green stools containing mucus but no blood for ten days. There had been a discharge from the eyes for eight days, and the child had been feverish and had vomited frequently for four days before entry. She had been fed a very dilute and inadequate formula of evaporated milk with a little rice starch added.

Examination.—Physical examination revealed a poorly developed, emaciated infant with dry, coarse, inelastic skin and very little subcutaneous fat. The epiphyseal and costochondral junctions were slightly widened. The eyelids were swollen and injected, the conjunctivae injected with small Bitot's spots and the corneas hazy with three small ulcers on the right cornea. The abdomen was distended, and the liver and spleen were palpable.

Examination of the blood revealed: hemoglobin, 90 per cent; red cells, 4,600,000; white cells, 16,850; polymorphonuclear neutrophils, 57 per cent; lymphocytes, 39 per cent; monocytes, 4 per cent. The urine was normal. The stools were green and contained no blood, mucus or pus; a culture was negative for pathogenic organisms. Roentgenograms showed marked rickets and advancing pulmonary tuberculosis.

Course.—The condition ran a stormy course with high irregular fever, continued diarrhea and progressive cough. The patient failed to respond to treatment and died two weeks after admission.

Necropsy.—There was extensive acute caseous tuberculosis of the lungs. No characteristic metaplasia was observed in any of the organs. The eyes were not available for histologic study. Definite rachitic changes were found in the ribs and in the long bones.

Comment.—The interesting feature in this case is that there was advanced active rickets associated with avitaminosis A. This suggests that osseous growth may continue if the deficiency of vitamin A is not too extreme.

CASE 3.—K. Y. C., a girl, was born in a hospital on Oct. 27, 1927. At birth she appeared to be normal, but shortly afterward persistent jaundice developed. She was fed whole lactic acid milk with 5 per cent carbohydrate added, approximately 140 calories per kilogram of body weight, but she gained slowly. When she was 1 month old, an abscess of the vulva, deeper jaundice and fever developed. The child ceased to gain weight and became emaciated. The liver and spleen became palpable. Shortly afterward she had pneumonia. When she was 7½ weeks old keratomalacia developed, and she was found to have congested conjunctivae, corneal ulcers with perforation and a prolapsed iris. There were marked leukocytosis and severe secondary anemia. The urine contained many pus cells but no desquamated epithelial cells.

The ocular symptoms gradually subsided under treatment with local applications and with the addition of cod liver oil to the diet, but she continued to do poorly. She had an ischiorectal abscess and repeated attacks of pneumonia, and finally she died on July 3, 1928, after an attack of diarrhea and pneumonia.

Necropsy.—Confluent lobular pneumonia was present. There was metaplasia of the epithelium of the uterine mucosa. The mucosa of the esophagus showed thickened epithelium with definite keratinization. Characteristic epithelial changes were not found in the mucosal epithelium of the trachea, bronchi, intestine, renal pelvis and urinary bladder.

Comment.—The condition of the patient is of interest chiefly from the point of view of etiology. She was given an adequate diet from birth, but in the presence of sepsis and probable impaired function of the liver keratomalacia developed. This subsided with local and general treatment. It was to be expected that there would be very little histologic evidence of avitaminosis A at the time of death, six months after the acute symptoms had subsided, and that such changes were found in the uterine mucosa is surprising.

CASE 4.—O. K., a girl aged 3 years, was brought to the hospital on Jan. 29, 1929. The child had measles two weeks before admission. The fever subsided

and she apparently was recovering, but five days before admission a white spot developed on the cornea of the left eye. With this came photophobia and lacrimation. Two days later a similar spot was noted on the right eye, and the temperature rose. The patient had a severe cough, a hoarse voice and a poor appetite for one week before entrance to the hospital.

She had been breast fed until the age of 2 years, after which time her diet had consisted of cereals with cabbage and a little meat. She had had no meat or green vegetables from the onset of measles.

Examination.—The physical examination revealed an undernourished child with a loose, dry, hot skin, acutely and critically ill. The conjunctivae were congested. The right cornea was hazy with a small opacity near the center, and the left cornea had sloughed off entirely, leaving the iris covered by a thin film of fibrinous exudate. Marked gingivitis, stomatitis, pharyngitis and extensive bronchopneumonia were present. The liver and the spleen were enlarged.

Examination of the blood revealed: hemoglobin, 80 per cent; red cells, 4,200,000; white cells, 23,500; polymorphonuclear neutrophils, 76 per cent; lymphocytes, 19 per cent; monocytes, 5 per cent; calcium, 9 mg. per hundred cubic centimeters, and phosphorus, 3.9 mg. Cultures gave negative results. Examination of the urine showed albumin + and very few white blood cells and epithelial cells. In the vaginal secretions there were no keratinized epithelial cells. Roentgenograms showed extensive bronchopneumonia but no evidence of rickets.

Course.—The patient was given supportive treatment and large doses of cod liver oil. The haziness of the right cornea cleared somewhat, but the child died four days after admission.

Necropsy.—Streptococcic septicemia and confluent lobular pneumonia were present. Very characteristic epithelial changes were observed in many organs. The entire laryngeal mucosa was replaced by thick, keratinizing squamous epithelium. The openings of the ducts of the mucous glands were completely or partially occluded by hyperplastic squamous epithelium. Similar changes were observed in the tracheal mucosa. The bronchi were dilated, and some of them were lined completely by a thick layer of keratinizing stratified squamous epithelium. In the pancreas two small ducts were lined by squamous epithelium. The mucosal epithelium of the tongue was markedly hyperplastic with very marked hyperkeratosis. The eyes were not available for study.

Case 5.—T. C. E., a girl aged 5 months, was brought to the hospital on June 10, 1926. Two weeks before admission excessive lacrimation and photophobia developed. One week later white spots appeared on both corneas and spread rapidly. The child had been breast fed for one month and then was given from 5 to 10 cc. of condensed milk in 90 cc. of water every three hours. She gained weight slowly at first but lost it after the onset of the ocular trouble.

Examination.—Physical examination revealed a fairly well developed, undernourished infant. The temperature was 38 C., and the child was moderately ill. The epiphyses at the wrists were slightly enlarged. The conjunctivae were injected, and the exposed bulbar conjunctiva presented a dry leathery appearance. The corneas were dry and opaque. No other abnormal findings were noted.

Examination of the blood revealed: hemoglobin, 78 per cent; red cells, 3,900,000; white cells, 21,500; polymorphonuclear neutrophils, 59 per cent; lymphocytes, 41 per cent. Examination of urine taken on admission gave normal results.

Course.—The patient had irregular fever with diffuse bronchopneumonia. The ocular lesions subsided under treatment, but the general condition failed to respond to treatment. Pneumonia became more severe, and just before the child died

pyelonephritis developed with albumin and many pus cells in the urine. A culture of the urine yielded B. dysenteriae. The patient died three and one-half weeks after admission.

Necropsy.—Extensive confluent lobular pneumonia was observed. No characteristic epithelial changes were present in any of the organs except the eyes. Superficial layers of the corneal epithelium were covered by a thick layer of keratinized epithelium. The tunica propria of the cornea was vascularized and infiltrated by round cells and leukocytes. The condition of the ribs and of the long bones evidenced typical well advanced rickets.

Comment.—The absence of characteristic epithelial changes in the internal viscera may mean either that these lesions have never developed or that they have yielded to treatment more readily than the ocular lesions.

CASE 6.—F. J. L., a youth aged 18, came to the hospital on April 22, 1929. He had a cough, raising thin yellow sputum, for four or five years, and it had become worse in the last year. Two months before admission mild night blindness and swelling of the feet developed. Ten days later his eyes became inflamed and rapidly lost their vision. One month later he became feverish and complained of intermittent abdominal pain and diarrhea. He passed from ten to twenty loose stools a day. Diarrhea, fever and cough continued until the time of admission. The diet consisted of cereals, bean sprouts and cabbage.

Examination.—Physical examination revealed a well developed, emaciated man, critically ill. The skin was dry and slightly scaly, with many comedones and slight hyperkeratosis of the hair follicles. The eyes were inflamed, with markedly pigmented, injected conjunctivae and opaque, necrotic corneas. The teeth were dirty, and there was marked pyorrhea. The lungs showed advanced tuberculosis.

Examination of the blood showed: hemoglobin, 43 per cent; red cells, 1,800,000; white cells, 8,000; polymorphonuclear neutrophils, 65.5 per cent; lymphocytes, 31.5 per cent; monocytes, 3 per cent. Examination of the urine showed a faint trace of albumin and a few white blood cells. The stools contained mucus, pus and hookworm ova. Roentgenograms showed advanced pulmonary tuberculosis with formation of cavities.

Course.—The patient had high, intermittent fever. He continued to grow weaker and died three weeks after admission.

Necropsy.—There was pulmonary tuberculosis with caseous pneumonia. The eyes showed healed ulcers in the corneas. The epithelium lining the corneas was of the squamous type with keratinization. The tunica propria of the corneas was replaced by a thick layer of vascular connective tissue and infiltrated by many round cells. No other characteristic epithelial changes were seen.

CASE 7.—F. Y. C., a boy aged about 2 months, was brought to the hospital on Dec. 23, 1929. He had been admitted to a local orphanage the evening before and was found to have a bloody discharge from both eyes. The history was unknown.

Examination.—Physical examination showed a well developed and well nourished infant, critically ill. The skin was hot and dry. Both eyelids were macerated and covered with a dense white membrane which overlapped the margin of the lids. The corneas showed fibrinopurulent masses of exudate. The eyes were hypo-esthetic on manipulation. There were mild laryngitis and a slight purulent discharge from the umbilicus.

Examination of the blood revealed: hemoglobin, 60 per cent; red cells, 3,800,000; white cells, 41,050; polymorphonuclear neutrophils, 74 per cent; lymphocytes, 24 per cent; monocytes, 2 per cent. Examination of the urine showed albumin ++, occasional epithelial cells, clumps of white blood cells and cellular casts. Virulent B. diphtheriae grew on cultures of material from both eyes and from the throat and of the umbilical discharge.

Course.—The patient failed to respond to a diet rich in vitamins and to general supportive treatment. He died four days after admission.

Necropsy.—Diphtheritic infection of the throat was present. The corneas of both eyes had sloughed off completely with formation of vitreous abscesses. No other characteristic changes were found.

Comment.—The diagnosis of the condition of this child is somewhat in doubt. It is certain that he had diphtheritic conjunctivitis; also, he was a well nourished infant with few signs of deficiency disease other than the ocular condition. However, the complete destruction of the eyeballs and the striking loss of sensitivity of the conjunctivae are phenomena not commonly associated with diphtheria. The finding of other foci of epithelial metaplasia would have confirmed the diagnosis of avitaminosis A beyond doubt. But the absence of such foci cannot be taken as conclusive evidence that the deficiency did not exist (cases 2, 5, 6 and 9).

Case 8.—S. S. T., a boy aged 3 years, was brought to the hospital on Oct. 12, 1929. He had had diarrhea with from four to ten loose mucoid stools a day for four months. Ten days before admission the diarrhea became worse and fever developed; appetite was lost, and the patient was unable to open his eyes. Red spots appeared on the face and extremities five days before admission. The diet consisted of cereal and bread with occasional small portions of meat and vegetables.

Examination.—Physical examination revealed a well developed, emaciated child, critically ill. The skin was dry and inelastic from the loss of subcutaneous fat and dehydration. A number of purpuric spots presented themselves over the extremities and abdomen. The eyes were sunken, and the conjunctivae were injected and dry. The corneas were hazy, with several small ulcers. There was slight edema of the feet.

Examination of the blood revealed: hemoglobin, 85 per cent; red cells, 5,000,000; white cells, 15,800; polymorphonuclear neutrophils, 85 per cent; lymphocytes, 11 per cent; monocytes, 4 per cent; culture, no growth; calcium, 8.7 mg. per hundred cubic centimeters; phosphorus, 3.2 mg.; albumin, 1.68 Gm.; globulin, 2.89 Gm. Examination of the urine showed albumin +, a few epithelial cells and hyaline and granular casts. The stools were semiliquid and contained blood, mucus and pus; a culture showed B. dysenteriae, mannitol-fermenting group. Roentgenograms of the chest and the extremities showed a normal picture.

Course.—The patient did not respond to general supportive measures and a liquid diet high in vitamins. Keratomalacia progressed. Pneumonia developed and the patient died one week after admission.

Necropsy.—Chronic ulcerative dysenteric colitis and confluent lobular pneumonia were present. The tracheal mucosa showed a few small foci of early metaplastic changes of the epithelium. The ducts of the mucous glands were dilated and partially occluded by a thick hyperplastic lining epithelium which was partly

squamous. The epithelium covering the esophagus showed extremely marked keratinization. Some of the ducts of the esophageal glands were completely obstructed by keratinizing squamous epithelium. In one area a fairly large abscess was found in the wall of the esophagus.

CASE 9.—T. H. L., a boy aged 9 months, was brought to the hospital on Aug. 8, 1929. Three weeks before his admission severe watery diarrhea developed, and he began to vomit food. One week later opacities were noted in both corneas. Vomiting and diarrhea improved, but the ocular lesions became progressively worse. The child had been breast fed all his life and had been given some rice porridge and noodles. The mother's diet was not known.

Examination.—Physical examination showed a well developed, well nourished infant, critically ill. The skin was dry and inelastic from dehydration; there was a small ulcer over the occiput. The eyes were sunken and the conjunctivae injected. The corneas were opaque and showed extensive ulceration. B. xerosis was present in the scrapings from the conjunctivae. Examination otherwise gave normal results. The patient died a few hours after admission.

Necropsy.—Characteristic metaplasia of the epithelium was found only in the eyes and in the esophagus. The corneas showed a large central perforation; the adjacent tissue was edematous and necrotic. Very little inflammatory reaction was noted in the surrounding tissue. The mucosa of the esophagus showed slight keratinization. One of the ducts of the esophageal glands showed hyperplasia and metaplasia of its lining epithelium.

CASE 10.—L. C. C., a boy aged 5 months, was brought to the hospital on April 20, 1929. He had been unable to open his eyes for eight days and had a moderate discharge from the eyes and increased lacrimation. The informant knew nothing more about the patient.

Examination.—Physical examination revealed an emaciated, dehydrated and critically ill infant. The eyes were sunken. The conjunctivae were injected, and the corneas were entirely destroyed and replaced by a thick fibrinous exudate. Scrapings from the conjunctivae showed B. xerosis and pneumococci in large numbers. There were no other abnormal findings. The calcium content of the blood was 9 mg. per hundred cubic centimeters, and the phosphorus content, 3.86 mg. The patient failed rapidly and died shortly after admission.

Necropsy.—The corneas of both eyes were extensively ulcerated, and in certain areas they were perforated and there was prolapse of the iris. The epithelium covering the corneas showed marked cornification. The trachea and the renal pelvis each showed a few small areas of epithelial metaplasia. The ribs and the long bones were slightly rachitic.

CASE 11.—W. N. Y., a girl aged 7 weeks, was brought to the hospital on Nov. 3, 1932. She was the eleventh child in the family and the seventh to be afflicted with similar symptoms. She had been breast fed from the time of birth. The mother's diet consisted of cereals, bread and boiled fresh vegetables but no meat or eggs. When the patient was 3 weeks old she began to vomit occasionally. When she was 6 weeks old, one week before admission, she began to have reddening of the eyes with a mucopurulent discharge. The day before admission she had four generalized convulsions.

Examination.—Physical examination revealed a well developed, well nourished infant, slightly drowsy. The anterior fontanel was full and tense. The eyes were swollen. The diagnosis was purulent conjunctivitis. The corneas were hazy and contained several small ulcers. The tendon reflexes were exaggerated and there was marked ankle clonus.

Examination of the blood showed: hemoglobin, 102 per cent; red cells, 4,500,000; white cells, 10,850; polymorphonuclear neutrophils, 55 per cent; lymphocytes, 42 per cent; monocytes, 3 per cent; calcium, 10.4 mg. per hundred cubic centimeters; phosphorus, 5.7 mg.; albumin, 2.82 Gm., and globulin, 1.73 Gm. The Wassermann test gave negative results. The spinal fluid was normal. Examination of the urine gave negative results. Roentgenograms of the skull and extremities showed a normal picture.

Course.—The patient was given a diet high in vitamins. Ocular symptoms cleared promptly, but convulsions continued. Two months later pneumonia developed. At this time the blood proteins were normal and the Wassermann reaction was still negative. The patient died three months after her first admission.

Necropsy.—Lobular pneumonia was present. No characteristic epithelial changes were found in any organ. The brain was normal.

Comment.—The family history of this patient is of considerable interest. The mother had an inadequate diet, and 7 of her 11 children died of similar symptoms. While no lesions were demonstrable in the brain, it is certain that the child was suffering from avitaminosis A. We were led to wonder if the absence of this factor from the mother's diet during pregnancy may have caused lesions of the nervous system that were irreversible and that were the cause of the neurologic symptoms. No such lesions have been reported in experimental animals, but to our knowledge no study of the effect of avitaminosis A on the central nervous system of the fetus has been made. The nervous lesions reported by Mellanby, by Hughes and his co-workers and by others have been of a different type.

CASE 12.—K. L. T., a girl aged 3 months, was brought to the hospital on Oct. 27, 1930. The father had syphilis, and the mother had had two miscarriages. A rash developed on the baby's skin two weeks before admission, and it gradually increased, being generalized one week later. She had been breast fed for one month, after which her diet consisted of rice porridge, bread, noodles and sugar water. No milk, eggs or other sources of vitamins were given.

Examination.—Physical examination revealed a poorly developed, emaciated infant with a dry, inelastic, leathery skin. A maculopapular cutaneous eruption covered the whole body. There was a mucopurulent discharge from each eye. The conjunctivae were injected and the corneas hazy, and the right one contained a small ulcer. The liver was greatly enlarged.

Examination of the blood revealed: hemoglobin, 95 per cent; red cells, 4,900,000; white cells, 27,000; polymorphonuclear neutrophils, 82 per cent; lymphocytes, 14 per cent; monocytes, 1 per cent; Wassermann reaction, negative; calcium, 5.7 mg. per hundred cubic centimeters, and phosphorus, 2.7 mg. The spinal fluid was normal. Examination of the urine showed a trace of albumin, many white blood cells and a few epithelial cells. Roentgenograms of the extremities showed a normal picture.

Course.—The rash subsided under antisyphilitic treatment, though a symptomatic purpuric rash developed after each injection of sulpharsphenamine until this drug was discontinued. The patient was given a diet rich in vitamins, but this was without effect. Keratomalacia progressed. Several subcutaneous abscesses developed, and the child died three weeks after admission from terminal bronchopneumonia.

Necropsy.—Confluent lobular pneumonia was present. The only epithelial change was found in the renal pelvis, where there were a few small metaplastic foci. The eyes were not available for histologic study.

CASE 13.—F. L., a girl aged 5 months, was brought to the hospital on Dec. 2, 1930. She had an impetiginous cutaneous lesion two weeks before admission. Five days later she had fever for two days and was given some unknown medication, after which she had from 3 to 4 loose stools a day. Five days before admission she began to keep her eyes closed all the time, and two days later a white opacity was noted on the right cornea. This increased in size. The past history was unknown save that she was breast fed and given a carbohydrate supplement until ten days before admission. After that she had a small amount of cow's milk.

Examination.—Physical examination revealed an underdeveloped, emaciated infant, drowsy and very ill. The skin was hot and dry, with an extensive red, subacute papular dermatitis and several impetiginous lesions of the scalp and ears. The eyes were closed. The conjunctivae were injected, and the corneas dry and opaque, with deep ulcerations. There was a general enlargement of the lymph glands. The spleen was palpable.

Examination of the blood showed: hemoglobin, 80 per cent; red cells, 4,100,000; white cells, 8,600; polymorphonuclear neutrophils, 12 per cent; lymphocytes, 87 per cent; monocytes, 1 per cent; albumin, 2.57 Gm. per hundred cubic centimeters, and globulin, 1.98 Gm. The urine contained a faint trace of albumin, and many white blood cells. Roentgenograms of the extremities and chest showed a normal picture.

Course.—The patient had a high swinging fever throughout her stay. She took feedings poorly, failed to respond to dietetic and supportive treatment and died two weeks after admission.

Necropsy.—Extensive bronchopneumonia was present. The corneas of both eyes were completely destroyed. There were endophthalmitis and purulent uveitis. Epithelial metaplasia was not seen in any organ except the renal pelvis.

CASE 14.—W. N. E., a boy aged 4 years, was brought to the hospital on Aug. 4, 1930. Three months before admission he had measles. After this, he had from four to ten green mucoid stools a day. His appetite was poor, and there was much loss of weight. Fever in the evening and a dry cough persisted for one month before admission. For ten days there had been corneal opacities. The diet consisted of millet, rice and bread, with occasionally a little meat and vegetables.

Examination.—Physical examination showed a well developed, emaciated, weak boy with a dry, inelastic skin. The conjunctivae were injected and pigmented, with wrinkling of the bulbar portion. The corneas were opaque with perforated ulcers. Extensive bilateral bronchopneumonia was present.

Examination of the blood revealed: hemoglobin, 68 per cent; red cells, 3,200,000; white cells, 13,400; polymorphonuclear neutrophils, 60 per cent; lymphocytes, 35 per cent, and monocytes, 5 per cent. The stools were soft and yellow, with pus and mucus.

Course.—The patient failed rapidly and died the day after admission.

Necropsy.—There were purulent bronchitis and extensive lobular pneumonia. Almost the entire tracheal mucosa was replaced by keratinizing squamous epithelium, which extended into the ducts of the tracheal glands and into the larger bronchi. The esophagus and the ducts of esophageal glands showed fairly marked metaplasia with occlusion of some of the ducts. The renal pelvis showed a few

areas of metaplastic change. In the prostate a few small masses of metaplastic squamous cells filled the glandular lumens. The eyes were not studied.

CASE 15.—M. C. S., a man aged 32, came to the hospital on Sept. 12, 1933. His illness began insidiously with swelling of the legs and shortness of breath five months before. Two months later the abdomen became distended. The patient had dysentery for six weeks and night blindness for three weeks before entry. He had suffered from anorexia and had eaten very little throughout his illness.

Examination.—Physical examination revealed an emaciated, prostrated man with marked ascites and pitting edema of the extremities. The eyes showed bilateral xerophthalmia with pigmentation and xerosis of the conjunctivae and of the corneas.

Examination of the blood showed: hemoglobin, 73 per cent; red cells, 3,700,000; white cells, 3,840; polymorphonuclear neutrophils, 85 per cent; lymphocytes, 9 per cent; monocytes, 6 per cent; albumin, 1.42 Gm. per hundred cubic centimeters, and globulin, 2.25 Gm. The urine contained very few white blood cells. The stools were liquid and yellow and contained blood, pus and mucus; a culture showed B. dysenteriae, mannitol-fermenting group. Roentgenograms of the chest showed a normal picture. The ascitic fluid was transudate.

Course.—The patient was given a liquid diet with halibut liver oil, 15 drops (0.25 cc.) per day. The condition of the eyes cleared completely in one week, but the general condition failed to respond to treatment. The patient refused all food and medication and died five weeks after admission.

Necropsy.—Chronic ulcerative dysenteric colitis was present. Characteristic epithelial changes were not seen in any organ. The eyes were not available for histologic study.

Comment.—The condition of this man is of exceptional interest from the standpoint of therapy. With 15 drops (0.25 cc.) of halibut liver oil a day his ocular lesions cleared, and his vision improved within a week. Nor was there a recurrence of ocular symptoms when his general condition became much worse. At necropsy there were no changes characteristic of avitaminosis A elsewhere in the body. It is doubtful if less concentrated forms of vitamin A would have been as effective in relieving avitaminosis in the presence of severe dysentery.

CASE 16.—H. H. C., a man aged 23, came to the hospital on Sept. 21, 1933. Three weeks before admission he had dysentery with from twelve to fifteen bloody mucoid stools a day. He lost his appetite but had no fever. The man had been a beggar for three years, and presumably he had a very inadequate diet.

Examination.—A well developed, emaciated and dehydrated man with loose dry skin was observed. The eyes were normal. There were no other remarkable findings.

Examination of the blood revealed: hemoglobin, 90 per cent; red cells, 4,500,000; white cells, 7,200; polymorphonuclear neutrophils, 72 per cent; lymphocytes, 24 per cent; monocytes, 4 per cent. The urine contained albumin + and many white blood cells. The stools contained blood, pus and mucus; culture showed B. dysenteriae (Shiga).

Course.—The patient was given the usual dietary and supportive treatment for bacillary dysentery. The stools improved somewhat, but the temperature rose continuously. The patient died two weeks after admission.

Necropsy.—Acute ulcerative dysenteric colitis and fairly extensive disseminated tuberculosis were present. Marked metaplastic changes were found in the trachea and in some of the larger bronchi. No such changes were noted elsewhere. The eyes were not studied histologically.

Comment.—In this case metaplastic changes were found only in the respiratory system, and there was no gross evidence of changes in the eyes. This then raises the question whether metaplasia of epithelium alone is pathognomonic for the diagnosis of avitaminosis A. As metaplasia of epithelium is frequently seen in chronic inflammations of long standing, such as chronic endocervicitis, chronic bronchitis and bronchiectasis, it seems that the diagnosis of avitaminosis A is to be made only after the factor of chronic inflammation is ruled out. However, in this case there is good evidence of vitamin A deficiency.

CASE 17.—L. J. K., a boy aged 14 months, was brought to the hospital on May 20, 1934, dead. He had been cared for in a local orphanage and had been given an adequate diet until he was 6 months of age. Thereafter, at home, he had been given a diet consisting entirely of rice powder and water with no other food. He had failed to grow, and one month before he was brought to the hospital ocular signs of keratomalacia appeared. He was treated in another institution by local instillation of "eye drops" but without dietary regulation. The eyes improved slightly, but the general condition became more critical, and the baby died on the way to the hospital.

Necropsy.—Extensive ulceration of the ocular cornea with perforation was observed. But the characteristic epithelial changes were not found anywhere else, except in the larynx in which there were a few small areas of epithelial metaplasia. The buccal and nasal mucosa showed no characteristic lesions.

As a result of our studies, we feel that ocular symptoms may be very early or late manifestations of vitamin A deficiency. The same is true of epithelial metaplasia in other sites. In many cases epithelial changes will be found to be scattered diffusely throughout the internal viscera and in the skin; in others these changes will be localized to one, two or three sites. This fact is exemplified by the patients studied by Blackfan and Wolbach [12] as well as by our own patients. We are unable to explain this extreme variability and have no hypothesis to offer save that the changes may be due to the accentuation or diminution of the pathologic process in various sites as a result of the presence or absence of associated deficiencies. As stated previously, these patients almost invariably are suffering from multiple deficiencies, and in no two of them are these deficiencies apt to be comparable. In experimental animals in which a single factor can be varied in the diet, the effects of this factor can be studied with precision. In patients who select their own diet, this is impossible. Consequently it will be possible to give the exact histologic sequences and relationships in human avitaminosis A only after a very large series of patients has been studied in detail. This

can be done best by the cooperative efforts of an ophthalmologist, an internist and a pathologist in a center in which vitamin A deficiency is endemic.

SUMMARY

The histories of 203 patients with avitaminosis A and the pathologic material from 17 autopsies and from 22 biopsies on these patients have been studied. The findings have been discussed from the standpoints of etiology, pathology, symptomatology, physical examination and diagnosis. An attempt has been made to correlate the clinical and pathologic pictures.

Pediatric Biographies

KARL FRIEDERICH OTTO WESTPHAL
1833-1900

A NOTE ON THE HISTORY OF PERIODIC PARALYSIS

JOHN RUHRÄH, M.D.†
BALTIMORE

Karl Friederich Otto Westphal was born in Berlin on March 23, 1833, the son of a prominent physician of the same name. He studied medicine in Berlin, Heidelberg and Zurich. In 1857 he was made an assistant in the smallpox division of the Charité Hospital in Berlin, and in the following year he became assistant physician in the department for the insane in the same institution, where he worked under such men as Griesinger, van Horn and Ideler. In 1861 he became a privat-docent in psychiatry in the University of Berlin, and in 1868 he was given charge of the smallpox division and of the department for internal diseases. In 1869 he was made professor ex officio in psychiatry and director and clinical teacher of the department for mental and nervous diseases, and in 1874, *ordentliche* professor of psychiatry. He was also made a *Geheimrat* in medicine. He contributed many articles to *Virchows Archiv für pathologische Anatomie und Physiologie*, the *Charité-Annalen* and many other journals, including the *Archiv für Psychiatrie und Nervenkrankheiten*, which he edited. His contributions are too numerous to mention, but one cannot pass over "Ueber einige durch mechanische Einwirkung auf Sehnen und Muskeln hervorgebrachte Bewegungserscheinungen." The Westphal-Piltz reaction is a contraction of the pupil associated with closure or attempts at closure of the eye. The Westphal-Strümpell neurosis or pseudosclerosis, also known as Wilson's disease, was described by the two men whose names it bears, after the Englishman Wilson had noted it. It is a rare disease characterized by bilateral degeneration of the corpus striatum and cirrhosis of the liver, marked tremor, spastic contractures, psychic disturbances and increasing weakness and emaciation, sometimes called progressive lenticular disease.

Westphal also described what is known as the paradoxical muscular contraction usually called by his name. His "Ueber das Verschwinden und die Localisation des Kniephänomens" is well known as is his work

† Deceased.

on the primary degeneration of the lateral columns of the cord. Numerous other contributions helped the progress of neurology and psychiatry. These include his description of agoraphobia in 1871, of the meaning of the knee jerk in 1875 and of pseudosclerosis in 1883. He died in 1900.

PERIODIC PARALYSIS

Periodic paralysis apparently was first described by Cavaré in 1853 and by Romberg in 1857, and twenty years later Hartwig described a case, but all these cases were associated with or followed malaria and the administration of quinine. Edward W. Taylor [1] has considered this early literature and prepared a bibliography. Of fifty-three cases, thirty-five occurred in three families: Cousot, five; Goldflam, nineteen, and Taylor, eleven. The onset always occurred before 24 years of age, most of the cases being in persons between 10 and 20 years of age.

C. Westphal described the first case in which malaria or the administration of quinine did not enter. His is a most extraordinary report and is entitled "Ueber einen merkwürdigen Fall von periodischer Lähmung aller vier Extremitäten mit gleichzeitigem Erlöschen der elektrischen Erregbarkeit während der Lähmung.[2]

. . . A twelve year old boy, paralyzed in all four extremities and the electric excitability of the muscles completely lost. This last aroused my greatest interest, and I suspected the electric apparatus more than the muscles.

The young patient was admitted to the clinic, January 7, 1885, for paralysis of all four extremities; it was not noted how long this had existed, but at any rate it disappeared. Late in the evening of January 19th there was another attack, but on the next morning movement was possible. . . . On the evening of the 30th there was a new attack of paralysis which on the 31st, except for slight movement of the hand, was complete. Observations made in the clinic showed a loss of electric excitability in the muscles. On the 30th the patient was turned over to the nerve clinic; the attack began to lessen, but voluntary movement was suspended with the exception of trifling finger and foot movements. When the limbs were raised they fell flaccidly; only once it seemed that the patient was able to hold the raised leg up. Taken out of bed he sank at once to his knees. After several hours the paralysis gradually left. No further exact examination was undertaken at this time.

In the night of the 5th of February after the patient had complained of pain in the calves of the legs in the evening, there was a fresh attack in which all four extremities were seized with pain about 4 o'clock in the morning; the patient then fell asleep and was all right in the morning.

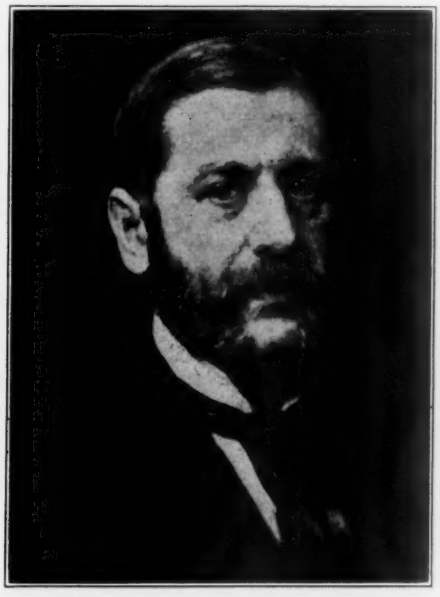
In the night of the 10th of February there was an analogous attack.

The examination of the boy during this time gave absolutely no evidence of disturbance in the nervous system nor in the other organs (namely, the spleen was not enlarged). For his age the boy was well developed; in the formation of the face there was a certain smallness of the lid opening. The cheeks showed a healthy redness. . . .

1. Taylor, E. W.: J. Nerv. & Ment. Dis. **35**:637, 1898.
2. Westphal: Berl. klin. Wchnschr. **22**:509, 1885.

[Dr. Oppenheim made some studies on the two attacks at night which were reported as follows:]

Attack 16-17 March. Patient, who some days before had diarrhea, complained on the afternoon of March 16 about 4 o'clock, that his right knee was so weak that he could not stand on a chair. An hour and a half later as he stood by the bed of another patient, he felt weak and he fell down. Then the arms became gradually weaker. He had at the same time in both legs and especially in the heels the feeling as if needles were being stuck in him. There was no such feeling in the arms. At the same time he had "frightful thirst" with an intense desire to urinate, but when he had the urine glass it was several minutes before he could do it.



KARL FRIEDERICH OTTO WESTPHAL
1833-1900

At 7 P. M. the assistant physician of the clinic confirmed the fact that the patient was not in a position to stand but on trying doubled up like a pocket knife. Of the voluntary movements there was some movement in the hips, but with the exception of a trifling amount in the left leg, bending and stretching at the knee or ankle were impossible. The movements of the arms were weak but not abolished.

At midnight, according to the patient, the paralysis reached the high point. Dr. Oppenheim saw the patient at 4 A. M. He was lying passively on his back, the sensorium entirely free, no disturbance in the muscles of the head, face or eyes. He only complained that turning the head could be made with difficulty and that he did not have strength to cough or sneeze. The upper and lower extremities were completely paralyzed, there was no trace of voluntary movement, passively raised limbs fell flaccidly. There was not a trace of stiffness or con-

tracture. Sensation normal over the entire body; the plantar reflexes were wanting, but the cremasteric and abdominal reflexes were present; knee jerks present. Respiration a little stressed but no dyspnea.

Electric excitability: with the strongest faradic current over the nerve of the upper and lower extremities which made the patient cry out there was only very weak twitching elicited. The current was tested on a healthy person and found very strong. The left peroneus nerve is not at all excitable, and there is no response on application over the muscle regions of the left peroneus.

At 8 o'clock in the morning the electrical reactions were again tested. From the nerves of the upper extremities, in which movement had improved, tolerably strong reactions were elicited, galvanic and faradic, direct and indirect. In contrast to this, moderately strong faradic currents elicited twitches so weak that they scarcely could move the extremities. Completely wanting were irritability of the peroneal nerve, the extensors of the foot and toes, the peroneal muscles contract but only very weakly. The results are achieved by the direct and indirect faradic current and also the galvanic current. The direct galvanic stimulation does not give any reaction to the leg extensors, while the calf muscles contract fairly well. When the contractions occur they are lightning like.

At nine o'clock in the morning the finger movements returned, and there were feeble movements of the extensors and flexors of the fingers and also of the ankle, as well as slight toe extension. The feet are in a strong equinus position. Pressure in abdomen good but patient cannot sit up in bed without help. The patient can turn the head but cannot put the head on the chest, backward movements of the head good. The face is unaffected and also movements of the eyes. Sensation in the lower extremities normal, passive movements of the legs were correctly oriented. The region between the back of the head and atlas sensitive on pressure. Plantar reflexes wanting even on deep needle thrusts, cremasteric and abdominal reflexes marked. No contraction of the muscles of the lower extremities on topping them and only trifling in the upper. Knee jerks are weak on both sides and do not follow every blow; no contraction of the calf muscles follows striking the Achilles tendon.

At 1 o'clock the patient could move all the extremities, although in the lower the movements were very weak, the faradic current caused contractions everywhere, even if weak, especially weak in the feet. The knee jerk on the right was absent or doubtful, on the left weak but clear.

Towards evening the patient could again walk, however felt weak in the knees.

In the evening rectal temperature 39.0, urine free from albumin and sugar.

On the following day, March 17th, the patient felt well, all the movements could be made only those in the left foot somewhat sluggish. On walking the front of the left foot dropped forward. The knee jerks were plainly elicited on both sides and that on a minimal irritation.

The electric irritability was normal everywhere, except in the left tibialis anticus muscle and the extensor digit. commun. in which the contractions were abnormally weak and with stronger currents only a trifling dorsal flexion be elicited as compared to the right.

In the course of the afternoon and evening the patient sweat a great deal and saw that in the attacks he felt hot and sweat. Rectal temperature 37.7. There is no enlargement of the spleen.

March 18. The electric irritability of the nerves of the lower extremities remains normal but there is an imperfect reaction on direct stimulation of the tibialis anticus muscle but there is no noticeable difference in the strength on moving the foot to left and right.

March 23. The patient complains that he cannot adduct the little finger of the right hand to the 4th finger; after half an hour this returned.

April 6. The faradic irritability of the nerves and muscles is good everywhere except the left tibialis anticus reacts less than the right although the voluntary movement is intact.

In the night of April 8th, that is at 2 A. M. on the 9th, Dr. Oppenheim was called to a new attack. The sensorium of the patient was entirely free, he said that he had had a profuse sweat and as he awakened he noticed that the paralysis had returned. He was of the opinion that it had not reached its height, as he could move the head freely and as he could still make trifling movements with the hands and the unpleasant sticking sensation had not begun. He had marked thirst.

The examination is as follows: The lower extremities are in a condition of complete, flaccid, total paraplegia; in the upper extremities voluntary movements are absent in the shoulders and elbows, while the hands and fingers can be moved tolerably well. The breathing is not essentially more rapid, costo-abdominal. Sensibility everywhere intact, on tendon irritation no trace of dorsal-flexion of the foot, knee jerks not clearly elicited (moreover the lighting was bad), pulse 96-100, rectal temperature 37.1. Only the faradic current could be used in testing. Over the crural nerve with the strongest current no clear response, and the same by direct stimulation in the quadriceps region; a questional ankle abduction from the peronei; not a trace of dorsal flexion, but painful extension of the toes; the same by direct stimulation.

By 7 o'clock in the morning of April 9, the paralysis had nearly entirely disappeared; the patient had slept and on awaking felt better. An examination under the same conditions as last night showed everywhere strong reactions. . . .

There follows a short further account of the same kind of attacks. The patient left the hospital in April and was seen again in June. The attacks were continuing and were somewhat more frequent, about one a week. Westphal offered no explanation for the attacks or the temporary loss of electric excitability of the muscles.

Pediatrics in Art

MOTHER AND NURSING CHILD

JOHN RUHRÄH, M.D.†
BALTIMORE

Primitive art has an interest and charm, whereas the same technic in the hands of modern sophisticated artists yields results which are unsatisfactory, as is evidenced by much of the modern art. The mother and child shown in the illustration is the work of some unknown member

Kwakiutl mother and nursing child.

of the Kwakiutl tribe of Indians, who are a branch of the Wakashan stock. They are now much reduced in number and are found chiefly on Vancouver Island. Their art is rated lower than that of the Haida people, who live farther north and who are known for the excellence of the carving on their totem poles. The child is seen nursing one breast and playing with the other, while the mother seems to be taking life very seriously. If this piece of work were exhibited in a modernistic exposition the sculptor would be hailed as the founder of a new school, and it would be given a fancy name.

† Deceased.

News and Comment

UNIVERSITY NEWS

Dr. Grover F. Powers, professor of pediatrics, Yale University School of Medicine, was given the honorary degree of Doctor of Science by Purdue University in June.

SOCIETY NEWS

Seventh Pan-American Congress on the Baby.—The Seventh Pan-American Congress on the Baby will be held on October 12 to 19 in Mexico City. Information may be obtained by writing to Dr. Alfonso Pruneda, Secretary Departamento de Salubridad, Esq. Paseo de la Reforma y Calle de Lieja, Mexico City.

Second Institute on the Exceptional Child.—The Second Institute on the Exceptional Child will be held at Langhorne, Pa., by the Child Research Clinic of the Woods Schools on Tuesday, Oct. 15, 1935.

Fifth International Conference on Child Health.—The Fifth International Conference on Child Health under the auspices of the Association Internationale de Pédiatrie Préventive will be held at Basel, Switzerland, on September 20 and 21 at the children's clinic of the university. Information may be obtained from Dr. D. Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

GENERAL NEWS

Postgraduate Course, University of Vienna.—The usual postgraduate course at the University of Vienna will be given this year between September 23 and October 5.

Bequests.—The Children's Hospital of St. Paul received $25,000 by the will of the late Leo Vogel of Mankato, Minn.

PERSONAL

Dr. F. W. Schlutz of Chicago delivered the principal address for the dedication of the new municipal children's hospital in Havana, Cuba, recently. The title of his address was "The Rôle of the Children's Hospital in Present Day Child Welfare."

DEATHS

Dr. William Ropes May of New York died on May 5, 1935.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

HYPERTROPHY OF THE ADRENAL GLAND FOLLOWING ADMINISTRATION OF PITUITARY EXTRACT. F. E. EMERY and WAYNE J. ATWELL, Anat. Rec. **59**:17, 1933.

Normal and castrated male rats were given injections of whole sheep pituitary extract. There was marked increase in the size of the adrenal gland, principally the cortex. Injections of antuitrin S produced no change in the adrenals of males or females.

SNELLING, Toronto, Canada.

THE RELATION OF VITAMIN A AND VITAMIN D TO URINARY CALCULUS FORMATION. A. RICHARD BLISS JR., G. R. LIVERMORE and ELSWORTH O. PRATHER JR., J. Urol. **30**:639, 1933.

The development of urinary calculi in albino rats appears to be related to a lack of vitamins A and D. Calculi were formed in 61.8 per cent of the rats maintained on diets deficient in vitamin A only. The calculi were composed chiefly of calcium phosphate and magnesium phosphate.

KUGELMASS, New York.

OBSERVATIONS ON THE CHEMICAL AND PHYSICAL RELATION BETWEEN BLOOD SERUM AND BODY FLUIDS: THE CHEMICAL RELATION BETWEEN SERUM AND EDEMA FLUIDS AS COMPARED WITH THAT BETWEEN SERUM AND CEREBROSPINAL FLUID. D. ROURKE GILLIGAN, MARIE C. VOLK and HERRMAN L. BLUMGART, New England J. Med. **210**:896 (April 26) 1934.

It seemed that a comparison of the distribution of substances between serum and edema fluids, which the authors have shown to be simple dialysates in a previous communication, with the reported distribution of substances between serum and cerebrospinal fluid would offer a basis for testing the validity of the dialysate theory of cerebrospinal fluid.

The authors found that the distribution of chloride, bicarbonate, inorganic phosphate, calcium, magnesium, nonprotein nitrogen constituents and reducing substances between serum and cerebrospinal fluid differs importantly from the distribution of these same substances between serum and edema fluids. The distribution of sodium differs only slightly. The factors which might explain these discrepancies in favor of the dialysate theory of cerebrospinal fluid were considered and found inadequate. The authors believe that cerebrospinal fluid is not a dialysate or a simple ultrafiltrate, and that the consideration of cerebrospinal fluid as a representative physiologic dialysate or ultrafiltrate has led to erroneous conclusions concerning the general physiologic diffusibility and chemical state of constituents of the plasma.

GENGENBACH, Denver.

OBSERVATIONS ON PLEURAL ABSORPTION. R. C. BROCK, Brit. J. Surg. **21**:650 (April) 1934.

This piece of experimental work was carried out on rabbits. Observations were made on both normal and inflamed pleura. Brock concludes from his work on the normal pleura that absorption of fluid from the pleura varies directly with the volume of fluid present, and that this absorption is influenced by the rapidity and depth of the respirations. This increased rate of absorption with a greater volume of fluid probably results from the fact that greater areas are in contact with the fluid. Also, the increase in the respiration results in a greatly increased circulation of both blood and lymph. In the inflamed pleura it was found that there

was a greatly increased absorption of fluid and thus there is a more rapid absorption of toxins. This absorption is increased in the acute stage because of the intense hyperemia, and the increased vascularity is responsible for this condition. When air is introduced into the inflamed pleural cavity the rate of absorption of fluid was at least doubled.

These findings are of practical value in the management of empyema, especially in children, when the rapidly accumulating fluid frequently leads to symptoms of distress. Brock suggests that aspiration should be practiced more often both to prevent accumulation and to give the maximum relief from dyspnea. In some cases aspiration even twice a day is advocated. This can be done by making a small opening in the intercostal space under local anesthetic, through which subsequent aspirations can be made without disturbing the patient and fear of spreading cellulitis in the wall of the chest.

SUMMERFELDT, Toronto, Canada.

SEASONAL RHYTHM OF THE BASAL METABOLISM OF THE PIGEON. L. DONTCHEFF and C. KAYSER, Ann. de physiol. **10**:285, 1934.

The basal metabolism of the pigeon depends on the temperature in which it lives. When the same birds were studied at 26 F. and at 30 F. there was noted a permanent increase of 10 per cent in the basal metabolism, which was caused by a prolonged stay in the cold. The effect of temperature is reflected in the basal metabolism during the year. A seasonal rhythm results, with an increase in the exchange during the winter months. The variations in the basal metabolism during the course of the year cannot be explained exclusively by the continued action of the average temperature of the atmosphere. Other factors, not yet established, are involved in determining such variations.

BUDSON, Detroit.

EFFECT OF SPLENECTOMY ON THE CALCIUM AND POTASSIUM OF THE BLOOD. L. BOUISSET and G. DUCLOS, Compt. rend. Soc. de biol. **113**:1358 (July 22) 1933.

Removal of the spleen in dogs produced the following: 1. There was practically no change in the alkaline reserve. 2. The plasma and total calcium varied little from the normal. 3. The potassium varied so irregularly that no conclusion could be drawn.

WAHL, Cleveland.

THE BLOOD CALCIUM AND POTASSIUM OF THE DOG AFTER TOTAL GASTRECTOMY. L. BOUISSET and G. DUCLOS, Compt. rend. Soc. de biol. **113**:1360 (July 22) 1933.

Venous blood was examined for chemical determinations at intervals for several days after gastrectomy in dogs, with the following results:

1. There was a diminished alkaline reserve in the first few days (from 52 to 46 mg.), on the average, with a return to normal in from two to three weeks. 2. Both the plasma and the total calcium diminished from 30 to 35 per cent, returning to normal in a variable time. 3. The potassium was lowered and returned to normal in the same ratio as the calcium.

It is concluded that gastrectomy in the dog does not permanently change the assimilation of calcium or potassium.

WAHL, Cleveland.

ANIMAL EXPERIMENTS WITH GOAT'S MILK ANEMIA. GRETE HAASE, Monatschr. f. Kinderh. **60**:241, 1934.

Haase fed goat's milk to white rats in order to study the resulting anemia. She found that rats under 35 days of age reacted much more severely than those aged 2 months or more. In the latter there was a tendency to spontaneous recovery. The anemia consisted of a reduction in red cells, with leukopenia and

lymphocytosis. The combined studies of the blood and pathologic studies suggested that the anemia results mainly from an inhibition of erythropoiesis.

Haase could not confirm the American observation as to the injurious effects of feedings of cow's milk on the blood of rats. In her series the goat's milk produced much greater damage.

Horse liver or copper alone did not cure the condition. Small doses of iron helped. Complete recovery followed the use of a proprietary liver preparation.

GERSTLEY, Chicago.

THE EFFECT OF THE INJECTION OF URINE FROM PREGNANT INDIVIDUALS UPON THE GROWTH AND UPON THE DEVELOPMENT OF DIFFERENT ORGANS IN NEW BORN PUPPIES. Y. MATSUURA, J. Orient. Med. **20**:77 (June) 1934.

For the first series of experiments 1 cc. of urine was injected daily for one week. The growth was unaffected in 53.3 per cent of the animals; in 26.7 per cent it was accelerated and in 20 per cent retarded. The development of the thymus was good, and increase in the cortex was seen in 50 per cent. The thyroid gland developed better than in the control animals, although there was no significant histologic change. The testes were slightly increased as compared with those of the control animals. In the other organs there was no significant change.

In the second series 5 cc. of urine was injected daily over a two and one-half week period. The general growth was unaffected in 40 per cent of the animals, increased in 26.7 per cent and decreased in 33.3 per cent. The thymus was atrophic. Atrophy of the cortex could be seen histologically in more than 50 per cent. The development of the thyroid was good; there was no significant histologic change. The testes were slightly larger than those of the control animals. The uterus was well developed; there were increase in the lumen, thickening of the mucous membrane, increase in glandular development and hyperemia. The breasts were increased in size and in the amount of glandular tissue, and there was a widening of the ducts. No significant changes were seen in the other organs.

AUTHOR'S SUMMARY.

DYE EXCRETION THROUGH THE LIVER AND KIDNEYS. YOSHIO YANO, Jap. J. Gastroenterol. **5**:123, 1933.

Acid dyes are excreted through the kidneys if they diffuse readily in serums. Of dyes excreted with difficulty by the liver and kidneys only the acid ones can be detected for a long period in the blood. The output of basic dyes is related to their affinity for red cells as well as their diffusibility in serums. Making lipoid solutions of basic dyes interferes with a direct relation between diffusibility and excretion.

KUGELMASS, New York.

EXCRETION OF DYES THROUGH THE LIVER AND KIDNEYS. YOSHINORI TADA, Jap. J. Gastroenterol. **5**:143, 1933.

Most dyes injected intravenously into dogs appear in the urine or bile. Diaminegoldgrün and dianiline black R do not appear. If dyes are excreted in both the urine and the bile they appear in the urine first. The more diffusible the dye the greater the concentration in the urine and the shorter the time before excretion. Dyes with low diffusibility pass the kidneys poorly, but the inverse is not always true. Ligation of the bile duct does not lead to compensatory excretion of such dyes as congo red 4 R by the kidneys unless both the liver and the kidneys tend to excrete the dye normally. In the latter case the maximum rate of excretion by the kidneys is not exceeded but the time is prolonged. On ligation of the blood supply to the kidneys the same relationships develop as from ligation of the bile duct. The concentration of dye in the blood and that in the urine and bile have a direct relation. For a specific dye the normal kidneys and liver have a fixed excretory power.

KUGELMASS, New York.

SIGNIFICANCE OF A CHANGE IN THE EMPTYING TIME OF THE STOMACH. O. CHRISTENSEN and A. L. SCHULTZ, Acta med. Scandinav. **81**:325 (March 6) 1934.

By collating the findings of previous and present-day authors it is shown that gastric retention six hours after a Kemp test meal must be considered a sign of disturbance of the function of the stomach. The tendency of the results of this test to vary with the subjective complaints of the patient makes it a valuable indicator of the effectivity of treatment.

Examination for gastric retention six hours after a Kemp test meal cannot be replaced efficaciously by roentgen examination five hours after a contrast meal. The latter method gives fewer positive results than the former in the same group of patients and does not tell any more about the severity of the stomach trouble when the results are positive.

KAJDI, Baltimore.

Nutrition

ON THE NERVOUS CONTROL OF LACTATION. HANS SELYE, Am. J. Physiol. **107**: 535 (March) 1934.

Selye summarizes the results of his experiments as follows:

The act of suckling maintains the mammary glands of the rat in the stage of active secretion over long periods, even though the galactophores are cut and the milk cannot be removed. Suckling at one set of nipples may maintain active secretion in other glands where suckling has been prevented by excision of the nipples. The physiologic involution of the mammary gland after weaning is thus conditioned by the withdrawal of the nervous stimulation of suckling rather than by the accumulation of the products of secretion in the gland. It is probable that the act of suckling stimulates the production of the hypophyseal hormone.

NOURSE, Cleveland.

THE NEW MECHANISM OF DEFENSE AGAINST BACTERIA THROUGH THE USE OF CERTAIN FOODS. LLOYD ARNOLD, Am. J. Pub. Health **24**:854 (Aug.) 1934.

Banana, apple and prune diets protected rats fed Bacillus enteritidis from diarrhea. Corn-starch and tomato diets were nonprotective. The mortality for mice on a banana diet was 6 per cent, as compared with 42 per cent for the mice on a corn-starch diet and 96 per cent for the group on the general stock diet.

KUGELMASS, New York.

THE EFFECTS OF ULTRAVIOLET IRRADIATION ON RACHITIC CHICKENS. G. M. HIGGINS, CHARLES SHEARD and R. M. WILDER, Anat. Rec. **58**:205 (Jan. 25) 1934.

Ultraviolet irradiation brought about healing of the rachitic changes in the bones of chickens. The blood calcium was brought to normal, though the phosphorus remained elevated. The thyroid, which had been hyperplastic, became normal, and the greatly enlarged parathyroid glands were reduced.

SNELLING, Toronto, Canada.

KETOGENIC DIET IN PEDIATRICS. L. CHARLES ROSENBERG, Arch. Pediat. **51**:273 (May) 1934.

A summary of the various diseases of childhood which have been treated by ketogenic diets is presented. Among the diseases which Rosenberg believes lend themselves to this form of therapy are epilepsy, infections of the urinary tract, calcinosis and scleroderma and high-strung and irritable conditions in children. The principles of ketogenic diets are discussed and their applications to the various subjects mentioned. The author particularly regrets the too infrequent use of this method of therapy in epilepsy.

WADDELL JR., University, Va.

NON-DIABETIC KETOSIS IN CHILDREN. OSCAR M. SCHLOSS, Bull. New York Acad. Med. **10**:183 (Aug.) 1934.

Under ordinary conditions of fat catabolism complete oxidation into carbon dioxide and water results, with occasional traces of ketone substances in the urine from the intermediary products of the oxidative process. Perversion of fat catabolism results in the accumulation of these ketone bodies, and a state of ketosis ensues.

While this condition is usually associated with severe forms of diabetes, in the child nondiabetic ketosis is not uncommon and may often threaten life. In adults, when the ratio of the metabolized fatty acid and dextrose exceeds 1.5, acetone substances appear in the urine. Experiments also show that in the child the threshold for ketosis is such that a ratio of 0.7 is sufficient to yield acetone. Children, therefore, require twice the amount of dextrose to metabolize completely a given amount of fatty acid. This explains the ease with which ketosis develops in children, manifested by a low storage of glycogen, a high metabolic rate, which is increased by fever, and a diminished intake of carbohydrate, due to poor appetite, vomiting of food or, frequently, both.

Ketosis in a mild form in the child is apparently without significance, since there may be no clinical symptoms. The severer forms, however, at times produce a threatening condition not dissimilar to diabetic ketosis and coma. These symptoms may be brought about by only slight provocation in some children, the same form manifesting few or no symptoms to those less susceptible. The symptoms may vary from slight drowsiness to severe coma and convulsions. The symptoms are always referable to the nervous system, with a special effect on the sensorium. The severe cases (with symptoms of coma, flushed face, red lips, air hunger, severe prostration) cannot be differentiated from cases of diabetic coma. Furthermore, these severe symptoms are not always of gradual onset, but may develop in the course of a few hours.

The tendency to severe ketosis is probably "an expression of a constitutional peculiarity of the individual, a magnification perhaps of the susceptibility of children in general, but at any rate, a metabolic fault which renders the child liable to severe ketosis provoked by conditions which are without effect on the ordinary person."

There is a detailed discussion of this important subject from both the laboratory and the clinical standpoint.

JAHR, Omaha.

GENERAL REVIEW OF THE PRESENT KNOWLEDGE OF THE VITAMINES. H. C. SHERMAN, Bull. New York Acad. Med. **10**:457 (Aug.) 1934.

A comprehensive evaluation of the present knowledge of the vitamins is submitted, including a discussion of the general principles and the specific functions of each group, with a consideration of the clinical and laboratory phases of each vitamin thus far studied.

JAHR, Omaha.

THE EFFECTS OF MODERATE DEFICIENCY OF VITAMINES. S. W. Clausen, Bull. New York Acad. Med. **10**:471 (Aug.) 1934.

Most clinicians are acquainted with frank deficiencies due to a lack or a marked diminution of intake of a specific vitamin. However, there are undoubtedly innumerable cases of moderate deficiencies characterized by mild or subclinical symptoms and signs of morbidity or symptoms not usually associated with the characteristic disease entity caused by an undersupply of the specific vitamin.

For example, evidence is accumulating that many cases of prematurity, immaturity and stillbirths are apparently associated with dietary insufficiency during pregnancy. Bizarre symptoms of many descriptions may be due to moderate deficiency of vitamin D or vitamin A. Vitamin C insufficiency (increased fragility of the capillaries, gingivitis, the prescorbutic anemia of infancy) may exist in areas where scurvy is rare.

The value of vitamin A as an anti-infective agent is discussed in some detail; Clausen based his conclusion on a study of 120 infants and an analysis of the histories of 700 older children. While large doses of vitamin A show no indication of lessening the incidence or severity of infection, it must not be supposed that a deficiency in this vitamin does not increase the susceptibility of the organism to bacterial diseases.

JAHR, Omaha.

REPORT ON VITAMIN D MILK BY COMMITTEE ON PUBLIC HEALTH RELATIONS. Bull. New York Acad. Med. **10**:507 (Aug.) 1934.

The report represents a study of the various phases of vitamin D milk in response to a request from the New York City Department of Health in an effort to regulate the production and sale of such milk.

In this communication there is a discussion of the reasons for this energized milk, the method of its production by the Zucker, Steenbock and concentration processes and its standardization, biologic control and general virtues as a potent antirachitic. There is also an outline of the physical, biologic and clinical tests. The following recommendations are made:

"Theoretically, it would be desirable for the producers to state on each bottle the number of units of vitamin D present in the milk, but in view of the fact that health departments have no laboratory facilities for assaying milk it is questionable whether this requirement would be practicable. It might perhaps, for the time being at least, be more desirable that the label merely state the source of vitamin D in each instance, the health department to decide what it considers a normal protective dose and in its license provisions demand proof from time to time that the milk produced under the license contains the stated dosage. From the evidence now available the Committee is of the opinion that such requirements will be satisfactorily fulfilled by:

"1. Directly irradiated milk containing 56 rat units per quart.

"2. Concentrate milk and yeast fed milk containing 100 rat units per quart."

From the standpoint of medicine and health, the committee sees no objection to permitting the addition of vitamin D to milk by any of the recognized methods under properly controlled conditions.

JAHR, Omaha.

VITAMIN D IN THE BLOOD AND MILK OF COWS FED IRRADIATED YEAST. R. F. LIGHT, L. T. WILSON and C. N. FREY, J. Nutrition **8**:105 (July) 1934.

Because of recent reports indicating that the vitamin A and D concentration in milk is directly influenced by the amount of the vitamin in the food and, in the case of vitamin D, almost directly proportional to the vitamin D content of the food, the authors were interested in determining the concentration of vitamin D in the blood as related to the concentration of this factor in the food and milk.

They were able to determine that the vitamin D present in irradiated yeast is practically completely absorbed. Their evidence points to a rapid disappearance of vitamin D from the blood stream at a maximum rate of 10 per cent per hour, followed by a decline in the rate of destruction as the concentration decreases. Other evidence reveals that the concentration of vitamin D in the blood plasma governs the concentration of this factor in the milk.

MUNNS, Winnetka, Ill.

ABNORMAL NUTRITIONAL STATES IN CHILDREN. BÉLA SCHICK and ANNE TOPPER, M. Clin. North America **17**:1219 (March) 1934.

Normal nutrition depends on the total daily metabolism, which has four components: (1) the basal metabolism, by which is meant the heat production when the body is at complete rest and during fasting; (2) the energy necessary for the muscular work; (3) the specific dynamic action of foods, which is the additional energy required for the ingestion of foods—a stimulus that is greatest for protein and least for fat; (4) the energy required in childhood for growth and development.

Under normal conditions, the nutritional requirements of the child are met when the caloric intake is sufficient for these four energy needs. If an excess is taken, it will be stored as fat. If less is taken, loss of weight occurs.

Schick and Topper discuss the causes of undernutrition and overnutrition and consider in detail the practical application of these physiologic principles to the treatment of such conditions.

In planning a diet for reduction of body weight the following factors should be considered:

1. The total caloric intake should be lowered to the basal requirements.

2. The level of the basal metabolic rate should be kept high by (*a*) a high protein content of the diet, (*b*) muscular activity and (*c*) thyroid extract, when the basal metabolism is low.

3. Limitation of the intake of salt and water.

4. Bulky foods for satiety.

In undernutritional states the following are indicated:

1. A high caloric intake covering the energy needs and greater than the basal requirements.

2. The basal metabolism should be kept at a low normal level by: (*a*) a low protein content in the diet, (*b*) decreased muscular activity and (*c*) phenobarbital in certain cases.

3. Insulin, if necessary, to stimulate the appetite.

4. A concentrated diet.

EUGENE SMITH, Ogden, Utah.

THE NECESSARY REQUIREMENTS IN A MINIMUM DIET FOR INFANTS AND CHILDREN. JOHN LOVETT MORSE, New England J. Med. **210**:1057 (May 17) 1934.

Morse suggests that the optimal diet for children appears to be one in which protein makes up from 10 to 15 per cent of the total caloric intake, carbohydrate from 40 to 60 per cent and fat from 30 to 35 per cent. The cheapest diet which will meet the nutritive needs is one in which 10 per cent of the total caloric intake is provided by protein, 60 per cent by carbohydrate and 30 per cent by fat. He suggests: that the absolute importance of vitamins cannot be overemphasized but that their relative importance is, however, being stressed altogether too much; that children still have sore eyes from other causes than a lack of vitamin A; that loss of appetite may be due to indigestion as well as to insufficiency of vitamin B; that he has never been able to restore the appetite by increasing the amount of vitamin B in the diet; that it is difficult to prove that a deficiency of vitamin C really diminishes resistance to infection in man; that in rickets a proper supply of available calcium and phosphorus is as necessary as vitamin D, and that a slight degree of rickets is not a serious condition; that if a child gets a reasonable amount of milk, an occasional egg, some meat and whole grains of cereal, he is very unlikely to lack vitamins. If the milk is not raw, a baby needs an antiscorbutic. It is a good thing for a child to have some vegetables as an additional safeguard. Spinach and other "leafy" vegetables are not, however, as necessary as many would lead one to believe. It is advisable to give babies vitamin D in some form during the winter months. He suggests that the food must contain certain salts in sufficient amounts, and that these salts must be present in such a form that they can be absorbed and utilized. The minimum diet is, therefore, the one diet which meets the child's needs, that is, the ideal or optimal diet.

GENGENBACH, Denver.

THE IMPORTANCE OF DISTURBANCES IN NUTRITION IN EDEMATOUS STATES. WARFIELD T. LONGCOPE, New England J. Med. **210**:1243 (June 14) 1934.

Protein is often grossly deficient in the diets of patients who suffer from these disturbances of nutrition. Diarrhea in addition is not uncommon, so that the protein deficiency may be still further increased by the difficulty of absorbing protein

through the gastro-intestinal tract or by the constant loss of small quantities of food protein and of blood in the stools. The deprivation of protein eventually leads to a lowering of the plasma proteins, which in turn predisposes to the formation of subcutaneous edema or is actually the cause of it. Accessory factors, such as the ingestion of considerable amounts of sodium chloride and water, the upright position and a mild degree of congestive heart failure may precipitate edema or exaggerate it, but the underlying cause rests usually in the deficit of protein. This particular form of deficiency may be relieved by feeding adequate or, if necessary, excessive amounts of protein. When this can be accomplished the plasma proteins may return to their normal levels and the edema may rapidly disappear.

GENGENBACH, Denver.

THE PELLAGRA-PREVENTIVE VALUE OF GREEN ONIONS, LETTUCE LEAVES, PORK SHOULDER, AND PEANUT MEAL. G. A. WHEELER and D. J. HUNT, Pub. Health Rep. **49**:732 (June 22) 1934.

Canned green onions contain the pellegra-preventive factor, but in small amounts. Canned lettuce leaves are poor in the pellegra-preventive factor. Lean pork shoulder is a good source of the factor, as is peanut meal.

SANFORD, Chicago.

UTILIZATION OF CALCIUM AND PHOSPHORUS FROM VARIOUS FORMS OF MILK AND MILK PRODUCTS. MARTHA M. KRAMER and RUTH MCCAMMON, Rep. Kansas Agric. Exper. Stat., 1932, p. 114.

The percentage of calcium in cheddar cheeses is approximately ten times that in soft cheeses, while the phosphorus is slightly more than twice that of soft cheeses. The phosphorus varies according to the amount of protein, while the calcium varies with the method of manufacture. There is no significant difference between the percentages of calcium and phosphorus in the rennet and in the acid types of cottage cheese. About 20 per cent of the calcium and 37 per cent of the phosphorus of the milk are retained in the soft cheeses, while 80 per cent of the calcium and 38 per cent of the phosphorus of the milk are retained in cheddar cheese. Rats fed rations containing milk products were superior to other rats in many ways and reproduced successfully. The efficiency of the utilization of calcium from the several dairy products tested will be reported later.

KUGELMASS, New York.

EFFECT OF SUNLIGHT ON VITAMIN D OF COW MILK. T. M. OLSON, South Dakota Agric. Exper. Stat., Ann. Rep., 1932, p. 15.

Milk from cows on pasture was richer in vitamin D and gave the greater gain of weight in rats, as compared with milk from "no-sunlight" cows with or without cod liver oil. Rats receiving milk in addition to cod liver oil showed the greatest gain in weight. The results obtained in the analysis of the blood of the several groups of rats were inconclusive.

KUGELMASS, New York.

EFFECT OF STORAGE ON THE VITAMIN C OF POTATOES. ELIZABETH J. MCKITTRICK and EMMA J. THIESSEN, Wyoming Agric. Exper. Stat., 42nd Ann. Rep., 1932, p. 25.

Approximately 5 Gm. is the minimum amount of Irish potatoes (raw or cooked) which protected guinea-pigs from scurvy. There was some loss after storage of from six to eight months. Cooking did not destroy the vitamin C, and in potatoes which had been stored for six months less cooked potato than raw was required for protection from scurvy. Potatoes grown under irrigation seemed to hold their vitamin C content during storage better than those grown without irrigation.

KUGELMASS, New York.

FURTHER OBSERVATIONS ON VITAMIN B_2. B. C. GUHA and P. N. CHAKRAVORTY, Indian J. M. Research **21**:211 (July) 1933.

The authors tested vitamin B_2 biologically. The unit was taken as the amount necessary when given daily to small young rats deficient in vitamin B_2 to produce a weekly gain in weight of 10 Gm. for a period of from two to three weeks. Of animal tissues, ox and buffalo kidney were found to be highest in vitamin B_2; fowl liver contains good amounts, but fish liver is poor in this vitamin. Extraction of vitamin B_2 is best done at p_H 5. Ox kidney loses considerable vitamin B_2 when heated on a water bath at p_H 10.5 for fifteen minutes.

SNELLING, Toronto, Canada.

XEROPHTHALMIA, TRIGEMINAL DEGENERATION AND VITAMIN A DEFICIENCY. E. MELLANBY, J. Path. & Bact. **38**:391, 1934.

Evidence is given which suggests that xerophthalmia produced in animals by diets deficient in vitamin A and carotene may be secondary to a loss of the neurotrophic control normally exerted on the cornea by the ophthalmic division of the trigeminal nerve. When xerophthalmia is present, the corresponding trigeminal nerve usually shows degenerative changes in the myelin sheaths, and in the rabbit their development is commonly almost synchronous. In early and slight xerophthalmia when the corneal epithelium becomes normal as the result of adding carotene or vitamin A to the diet, the nerve also becomes normal. In such cases the myelin degeneration is of the annular type, and although the fibers may be swollen the myelin does not invade the axis-cylinder. This type of nerve degeneration seems capable of rapid recovery. In more severe cases of xerophthalmia, in addition to degeneration of the annular type, many of the fibers show typical wallerian degeneration, the axis-cylinder being invaded by degenerated myelin, while globules of the latter are scattered throughout the nerve. In cases of this type recovery of the nerve fiber either does not take place or does so only after months of vitamin A or carotene therapy. The nerve cells of the gasserian ganglion, as well as their nerve fibers, show degenerative changes. Indeed, it is possible that the original lesion is in the cells, and that the trigeminal changes, peripheral and central, are secondary thereto. In the rat, in which as the result of vitamin A deficiency the eyelids become puffy, the cornea may escape xerophthalmic changes. In such cases also the trigeminal nerve shows demyelinization. Since degeneration of the afferent nerves is widespread in animals brought up under these experimental conditions, it is probable that hyperplasia and metaplasia of other epithelial and mucosal surfaces throughout the body and the subsequent invasion of these tissues by micro-organisms are also related to changes in their afferent nerve supply. FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.].

PERCENTAGE OF FAT IN HUMAN MILK. MARGARET F. LOWENFELD, SIBYL T. WIDOWS and HAZEL H. C. GREGORY, Lancet **1**:1003 (May 12) 1934.

Digital expression and gentle suction with a breast-pump used with pressure on the breast seemed to give the nearest approach to the nursing action of the infant, and were the methods of extraction employed. As a result of systematic comparison made by these two methods it was shown that pressure is the most important factor in producing a high percentage of fat. The greater the pressure the steeper the rise in the percentage of fat. Suction alone tended to lower the percentage.

After investigating the milk of fifty-one mothers and analyzing 294 specimens, the authors drew the following conclusion: In any given sample of milk, other factors being equal, the percentage of fat present depends inversely on the quantity of milk in the breast at the time of taking the sample and directly on the degree of pressure exerted on the areola and nipple in the process of extraction.

Observations on the percentages of fat obtained in samples of milk by different methods of extraction showed that the percentage of fat ingested even from the same breast varies considerably with different infants, a baby who is a vigorous

sucker being able to obtain a higher proportion of fat than the child who is a poor sucker.

The babies observed were put into two groups:

TYPE 1.—A small active baby showing dyspeptic symptoms such as vomiting and green stools. On inquiry and observation it was found that the baby was a vigorous sucker and the mother's milk supply plentiful. When boiled water was administered before and during the feeding and care was taken that the infant did not get the strippings of the milk the fault tended to be corrected.

TYPE 2.—The exact antithesis of type 1. This baby weighed above the average at birth, was contented and sleepy and yet failed as time went on to gain satisfactorily in weight, in spite of the fact that he ingested apparently adequate quantities of milk. In many cases of this type the supply of milk was abundant, but the musculature of the nipples was so lax that the milk tended to spurt from the breast before feeding and the baby was taking dripped milk, the lowest possible in fat for that mother.

LANGMANN, New York.

THE RÔLE OF THE LIVER IN THE METABOLISM OF CARBOHYDRATE AND FAT. C. H. BEST, Lancet **1**:1155 (June 2); 1216 (June 9), and 1274 (June 16) 1934.

This is a comprehensive statement of the present knowledge of this subject. The various topics discussed include fat, carbohydrate and phosphate metabolism in dehepatized animals, spontaneous hypoglycemia, liver function tests, fat tolerance curves and the distribution of glycogen and fat in the liver. Also included are discussions concerning epinephrine and glycogen in the liver and the relation of the anterior lobe of the pituitary body and fat and carbohydrate metabolism in the liver.

LANGMANN, New York.

VITAMIN C IN THE HUMAN PITUITARY. J. GOUGH, Lancet **1**:1279 (June 16) 1934

Among the methods which have been devised for the detection of ascorbic acid (vitamin C) is the histochemical test of Szent-Györgyi. Gough and Zilva found that the anterior lobe of the pituitary body in certain species—e. g., man, the ox and the dog—yielded a stronger Szent-Györgyi reaction than the adrenal. The pituitary body in the ox appears to be the richest of the known vitamin C-containing tissues and seems to be as rich as any of the well recognized natural sources of the substance, such as mango and paprika.

A series of one hundred human pituitary bodies were examined post mortem, and it was noted that the pituitary body in man invariably stains darker than the adrenal. Gough and Zilva also noted that there was a considerable variation in the intensity of the reaction in different persons, the intensity running roughly parallel to the state of nutrition. Also, the reaction was less intense in the aged than in younger subjects.

LANGMANN, New York.

A METHOD OF FEEDING CONCENTRATED MILK MIXTURES TO INFANTS. K. CAMPBELL, M. J. Australia **1**:557 (April 28) 1934.

Campbell reports gratifying results of feeding infants according to their caloric requirement rather than on specified high dilutions of milk.

TENNEY, Madison, Wis.

MAGNESIUM IN ANIMAL DIETS. I. J. CUNNINGHAM, New Zealand J. Sc. & Technol. **15**:191, 1933.

The concentration of magnesium in the blood serum and the bones of rats was increased by increasing the amount of this element in the diet. Magnesium carbonate produced the greatest effect of the different salts used. The total proportion of calcium in the dried bodies was not greatly affected by the feeding of magnesium. There was a general tendency to a lower blood calcium level. At the

higher levels of magnesium carbonate and magnesium sulphate the ash content of the bones decreased and moisture increased, but the interpretation was confused by diarrhea in the animals.

KUGELMASS, New York.

CHANGES IN ACID-BASE EQUILIBRIUM DURING PROGRESSIVE ASPHYXIA. D. CORDIER, Ann. de physiol. **10**:301, 1934.

Dogs were asphyxiated by depriving them of oxygen. The total carbonic acid of the arterial plasma diminished from the beginning of the asphyxia till death. The carbon dioxide was only slightly lowered in the early stages but was markedly lowered when death approached. The p_H of the arterial plasma suffered two changes. It was elevated during the first part of the asphyxia, at the same time that the total carbonic acid of the plasma was lowered. This simultaneous but opposite change in p_H and carbon dioxide is an index of gaseous alkalosis. Then the p_H was lowered, while the total carbonic acid indicated a state of acidosis caused by the fixed acids, the free carbonic acid of the plasma diminishing until respirations ceased.

In asphyxia caused by confinement, or rebreathing, the total carbonic acid of the arterial plasma increased progressively up to an advanced stage of the asphyxia, then diminished until death. If the asphyxia is maintained to a feeble concentration of oxygen, the total carbonic acid of the plasma can reach values below normal. This fall of carbonic acid indicates the production of a state of acidosis by the fixed acids under the influence of a lack of oxygen. The p_H in asphyxia by rebreathing fell rapidly when the value of the oxygen became sufficiently low, which indicates that to the gaseous acidosis caused by the accumulation of carbonic acid was added an acid intoxication caused by a lack of oxygen.

In these two types of asphyxia ventilation increases progressively in proportion to the diminution in the value of the oxygen in the air inspired. The ventilation diminishes rapidly several minutes only before respiratory arrest. It is difficult to admit a change in the sensitivity of the respiratory center under the influence only of the lack of oxygen when one studies comparatively the respiratory phenomena in the two types of asphyxia. The depression of respiration cannot explain the acidosis of asphyxia.

In the two types of asphyxia studied the animals succumbed when the value of the oxygen of the air in the chamber (100 liters) fell to about 3 per cent.

In asphyxia by lack of oxygen the value of the lactic acid increased during the total duration of the asphyxia. This increase was at first slight, then became rapid when death approached. In asphyxia by rebreathing the lactic acid showed two changes. It diminished during the first part of the asphyxia, then increased greatly just at the point of death, without attaining the values observed in asphyxia by lack of oxygen. The differences between the two types of asphyxia can be explained by the action of carbonic acid on the production of lactic acid. The results obtained on the entire animal confirm the phenomena observed on the isolated muscle.

BUDSON, Detroit.

ACTION OF IRRADIATED ERGOSTEROL ON THE BLOOD CALCIUM OF ANIMALS IN A STATE OF CHRONIC PARATHYROID INSUFFICIENCY. FRANZ MATHIEU, Compt. rend. Soc. de biol. **114**:1375, 1933.

Thyroparathroidectomized male dogs were kept alive by injections of calcium salts. Several months after the operation large doses of viosterol caused a small increase in the blood calcium, sometimes preceded by a slight decrease.

KUGELMASS, New York.

ACTION OF IRRADIATED ERGOSTEROL, PARTICULARLY FROM THE POINT OF VIEW OF DENTITION. PIERRON, Paris méd. **2**:107 (Aug. 4) 1934.

Pierron expresses the belief that in order to obtain good calcification of the teeth and to prevent dental caries, it is necessary to give phosphorus in conjunction with irradiated ergosterol.

LESLIE, Evanston, Ill.

EFFECT OF DIET ON THE TEETH. A. WILCKEN, Progrès méd., Sept. 1, 1934, p. 1374.

This article purports to be a brief review of the work of May Mellanby. Two principal factors are operative in dental caries: 1. The better the teeth are formed originally, the more resistant they are. 2. Independently of their structure, the resistance is influenced directly by diet. Foods containing vitamin D, such as egg, animal tissue, milk and cod liver oil, protect the teeth; cereals, such as oatmeal and bread, are said to favor the development of caries. LESLIE, Evanston, Ill.

ALCOHOL-EXTRACTABLE SUBSTANCES FROM RICE AND THEIR RELATION TO VITAMINS. C. SCAGLIONI, Arch. Ist. biochem. ital. **5**:303, 1933.

Substances extractable by alcohol from polished rice enhance the polyneuritic manifestations of beriberi, while extracts from whole rice attenuate and even cure these manifestations. Both extracts, when given together, shorten the period of the disease in pigeons. They are inactive, however, when the birds are kept on a vitamin-free diet. KUGELMASS, New York.

BUTTERMILK IN THE TREATMENT OF SEVERE NUTRITIONAL DISTURBANCES. M. M. DEL GIUDICE, Pediatria **42**:830 (July 1) 1934.

A brief historical review of acidified milks and a detailed consideration of the composition of and therapeutic indications for buttermilk are given in this paper. Cases of patients with autointoxication and marked malnutrition who throve on a diet of a type of desiccated buttermilk are reported.

SIGNORELLI, New Orleans.

NUTRITIONAL VALUE OF VARIOUS MILKS ON LARVAE OF THE FROG. P. LUSIANI, Pediatria **42**:845 (July 1) 1934.

This paper represents a report of studies revealing the action of the milk of several wet-nurses on the development of larvae of frogs. Luciani observed that in relation to the different characteristics of the nurses, as well as to the different quantities of thyroid hormone passed into the milk, there resulted in the larvae at first differences in metamorphosis and eventually differences in the total growth.

SIGNORELLI, New Orleans.

CORRECT FEEDING OF THE DYSTROPHIC INFANT. JUAN CÓRDOBA, But. Soc. catalana de pediat. **4**:177, 1931.

An adequate intake of food, both quantitative and qualitative, is necessary in treating the dystrophic infant. If the appetite is poor, concentrated feedings are recommended, with fluids between meals. Diarrheas are to be treated according to the cause. WATSON, Elmhurst, Ill.

CONCEPTION, ETIOLOGY AND PATHOGENESIS OF HYPOTHREPSIA AND ATHREPSIA. MANUEL MIRALBELL, But. Soc. catalana de pediat. **5**:28, 1932.

Miralbell attempts to harmonize several of the leading classifications of nutritional disorders of the nursling. He explains the classification of Finkelstein and Czerny from a physiopathologic point of view. He objects to combining the terms atrophy and decomposition, one being an anatomic, and the other a physiologic, conception. Marfan's classification is followed in the main. The author proposes to specify in each diagnosis: (1) the etiology, or the cause that produced it or the principle that is in excess or is lacking, (2) the pathology, or the anatomic wounds which it causes and (3) the anatomic conditions of the child under which it is produced. WATSON, Elmhurst, Ill.

EXCRETION BY THE COLON. H. SALOMÓN, Rev. Soc. argent. de biol. **9**:223, 1933.

The water-soluble ash in human feces is 77 per cent of the total ash when extracted from fresh, and 84 per cent when extracted from dry, feces. This is considered the part excreted by the intestine, the insoluble ash being due to non-absorbed food. With diets rich in cellulose the water-soluble ash increases to two or three times the normal amount. Lipins and cholesterol also increase to three to four times the normal amount with such diets. The absorption bands of carotene and xanthophyll may still be found in feces after nine days of a diet lacking in those pigments.

KUGELMASS, New York.

MECHANISM OF THE ACTION OF A SALT-FREE DIET; DISTRIBUTION OF CALCIUM IN THE BLOOD. H. SCHWARTZ, Arch. exper. Path. u. Pharmakol. **173**:558, 1933.

A diet free from sodium chloride does not affect the total serum calcium of rabbits, but does cause an increase in the protein-bound calcium at the expense of the inorganic calcium. A diet rich in sodium chloride has the opposite effect. These findings are correlated with the anti-inflammatory effect of salt-free diets.

KUGELMASS, New York.

CARBOHYDRATE METABOLISM. E. G. WINTER, Arch. f. Gynäk. **154**:354, 1933.

Hypoglycemia exists in the mature new-born which may resemble a physiologic loss of weight caused by undernourishment. The assimilation of carbohydrates in the new-born is normally poor. The changes in the glycemic reaction were explained as being caused by unpreparedness in the transition from fetal to extra-uterine life. This transition period lasted to the second week of life.

KUGELMASS, New York.

INFLUENCE OF FOOD ON THE BLOOD SUGAR IN CHILDREN. ASPARUCH PANOFF, Monatschr. f. Kinderh. **60**:194, 1934.

Panoff tested the effects of protein, carbohydrate and fat on the blood sugar in a series of children, some suffering from nervous disease and some from diabetes. A considerable rise in the blood sugar follows an excess of carbohydrate. An excess of protein may lead to a late and very weak increase of the blood sugar, but this is by no means constant. Fat, on the other hand, often leads to a lower blood sugar curve.

GERSTLEY, Chicago.

FAT OF ABSORBED CARBOHYDRATES IN THE ORGANISM. HEINRICH SCHUR, ARTUR LÖW and ANTON KRČMA, Wien. Arch. f. inn. Med. **24**:463 (Feb.) 1934.

It was shown in the experimental animal that a single massive ingestion of carbohydrates leads to a marked increase of the depot fat. The glycogen content of the liver increases markedly in the small animal, sometimes beyond ten times the initial amount. The weight of the liver is almost doubled.

The effect of fat deposit can be particularly well demonstrated in the peritoneum. Of the ingested and absorbed carbohydrates, fully a third appear in the form of fat. About one fourth of the amount of ingested food is still found in the stomach seven hours after the intake.

The relatively high alimentary increase of the carbohydrate content of fatty tissue combined with demonstrable alimentary increase of fat in the total organism, with a relatively slight increase of fat content of the liver, would indicate that the change of carbohydrate to fat takes place mostly in fatty tissue.

Prolonged periods of inanition can interfere with the absorption of carbohydrates and particularly with its change into fat. Anorexia could be a consequence of such a dysfunction.

SCHLUTZ, Chicago.

RÔLE OF UNSATURATED ACIDS (LINOLEIC ACID) IN THE NUTRITION OF RATS. JENO BECKER, Mezogazdasagi Kutatasok **6**:363, 1933.

Rats need small amounts of fats containing linoleic acid. Ether extracts of walnuts of different degrees of ripeness were fed to rats in doses of 5 mg. The I numbers of the samples indicated different contents of linoleic acid. The more acid there was present, the better the growth obtained. As the feeding of only 5 mg. of walnut oil (from 2 to 3 mg. of linoleic acid) cured the new deficiency disease reported by Burr and his collaborators, it seems that linoleic acid acts as a vitamin.

KUGELMASS, New York.

BIOLOGIC ACTION OF VITAMINS. HANS VON EULER, Ark. kemi, min. geol. **11**B:6, 1933.

That vitamin A deficiency causes decreased resistance against infection was shown during an epidemic of disease among rats (due to Bacterium haemosepticum). Of seven hundred rats observed, only those that had received vitamin A in their diet escaped infection. Guinea-pigs on a vitamin C-deficient diet were subject to pneumonia even before scurvy was manifest, while control animals receiving vitamin C were not. Lemon juice must contain some substance other than ascorbic acid, because this acid alone is not sufficient to guard against infection. Studies in the periodic fluctuations in the growth of rats over a period of four years showed a maximum growth in March and April and a minimum growth from October to February.

KUGELMASS, New York.

Prenatal Conditions

SPINA BIFIDA OCCULTA AMONG JEWISH AND ARABIAN CHILDREN IN THE NEAR EAST. HENRY KELLER, M. Rec. **139**:450 (May 9) and 521 (May 16) 1934.

A study of 530 cases of spinal disorder among the Jewish and Arabian school children of the Near East showed that the people of the Near East are frequently affected by spina bifida occulta. The Jewish children appeared to suffer more from the deformity than the Arabian. Of 276 Arabian children examined spina bifida occulta was found in 52, while of 258 Jewish children 73 were found to be affected. In both groups males appeared to be more susceptible than females. In most of these cases there were other symptoms. Spina bifida occulta is discussed from a medicolegal aspect. Every patient suffering from spina bifida occulta must be considered as a potential invalid and should be cautioned against exposure of the back to undue stress or strain.

WILLIAMSON, New Orleans.

A CASE OF MULTIPLE CONGENITAL ANOMALIES OF THE MÜLLERIAN AND GENITO-URINARY SYSTEMS WITH ABSENCE OF THE COCCYX. JOHN L. NEWELL, New England J. Med. **210**:1217 (June 7) 1934.

In the case herein reported not only was there imperfect development of the right müllerian duct, but also the rudimentary uterus was outside the true pelvis and had no connection with the organs of the left müllerian duct. Furthermore, the right kidney and ureter and the perineal bodies, anal sphincter and coccyx were absent, and there was an anomalous band of peritoneum including the right round ligament and obliterated hypogastric artery.

GENGENBACH, Denver.

CONGENITAL SCOLIOSIS; A REVIEW OF SEVENTY-SEVEN PATIENTS. JOHN G. KUHNS, New England J. Med. **210**: 1311 (June 21) 1934.

Cases without demonstrable abnormalities in the spine were omitted from this series. Fifty-six girls and twenty-one boys were studied. There is little evidence to support the theory that these abnormalities are hereditary. The prenatal

histories revealed nothing unusual in any of the cases in which they could be obtained. Most of the curves were double curves; those with convexity to the right in the dorsal region and to the left in the lumbar region were the most common. There was one triple curve. The curvatures were noted at birth in only eighteen patients, during the first six months in eleven, before 2 years of age in nineteen and after 6 years of age in fourteen. No subjective symptoms were present in any of the cases.

Congenital scoliosis is never wholly cured except in the occasional patient with a mild deformity who is followed carefully from earliest infancy until growth is obtained. The greatest improvement in bodily symmetry and the correction of the scoliosis have been seen in those children who have been followed carefully since birth.

The most effective treatment was the use of a molded plaster shell which holds the spine in a slightly overcorrected position. Exercises have been given in practically all cases—mobilizing exercises to overcome contractures of the muscles and ligaments and postural exercises to secure better general muscular development. Treatment must begin early if good functional and anatomic correction is to be obtained. Supervision must be continued until full growth has occurred.

GENGENBACH, Denver.

CONCENTRATED FEEDINGS IN THE NUTRITION OF PREMATURE INFANTS. C. H. WEBB, South. M. J. **27**:608 (July) 1934.

Concentrated high caloric feedings were apparently well tolerated by premature infants. Two simplified, easily available formulas prepared with breast milk whenever possible are suggested. Eighteen premature or immature infants fed these formulas exclusively and twenty-eight infants fed them in addition to breast feedings, showed gains in weight above the usual for such infants.

Intramuscular injections of whole blood and subcutaneous injections of saline solutions are offered as a means of combating hemorrhagic manifestations and excessive loss of weight in the premature infant during the first days after birth.

The early administration of antirachitic agents and iron in adequate amount is stressed.

SCHLUTZ, Chicago.

THE PROPAGATION OF THE VIRUS OF INFECTIOUS LARYNGO-TRACHEITIS ON THE CHORIO-ALLANTOIC MEMBRANE. F. M. BURNET, Brit. J. Exper. Path. **15**:52, 1934.

The virus of laryngotracheitis may be propagated in the chorio-allantoic membrane of the developing egg. The lesions produced in the membrane are primarily due to proliferative and necrotic changes in the ectodermal layer; the proliferating cells frequently show typical intranuclear inclusions similar to those found in the tracheal lesions.

FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

DUODENAL STENOSIS FROM MALFORMATION OF THE PEDICLE OF THE LIVER. ROCHER, ROUDIL and COURRIADES, Ann. d'anat. path. **10**:277 (March) 1933.

An infant of 10 days had vomited from birth. Roentgenoscopy showed a dilated stomach the contractions of which failed to propel the barium sulphate farther in five hours. The child died on the operating table. Examination revealed adhesions of the duodenal mesentery and the mesentery of the transverse and ascending colon, accompanied by vascular anomalies. The portal vein lay across the duodenum and compressed it.

VINTON, Brooklyn.

CONGENITAL ABSENCE OF THE ANORECTAL CANAL. A. AMELINE, Bull. et mém. Soc. nat. de chir. **59**:356 (March 1) 1933.

In a case of imperforate anus an incision was made the second day of life over the tip of the coccyx, and the intestine was found and drawn down and

stitched to the skin. At 8 months roentgenoscopy showed a megarectum. Thirty treatments were given with diathermy, and the anal orifice was dilated progressively. At the age of 3 years and 8 months the child had had no inconvenience and no infectious disorder.

VINTON, Brooklyn.

RIGHT-SIDED DIAPHRAGMATIC HERNIA IN AN INFANT WITH GASTRO-INTESTINAL ANOMALIES. QUIVY and PANNIER, Bull. et mém. Soc. de radiol. méd. de France **22**:170 (March) 1934.

In the case reported the stomach was bilocular, with communication between the two chambers at the esophageal opening. The colon was very mobile, and its transverse portion was temporarily herniated through the same opening.

VINTON, Brooklyn.

PAINFUL TYPES OF LUMBOSACRAL SPINA BIFIDA OCCULTA AND THEIR TREATMENT. F. LAGROT and L. COHEN-SOLAL, Rev. d'orthop. **21**:193 (May-June) 1934.

The authors have not reached any conclusion regarding the possible cause of the pain in this condition. Laminectomy in their hands appears to give excellent results. In less severe cases epidural injections of iodized poppy-seed oil 40 per cent, sodium salicylate, roentgenotherapy and immobilization are used.

RYAN, Vancouver, Canada.

AUTOPSY IN A CASE OF CLEIDOCRANIAL DYSOSTOSIS. M. VAN NECK, Rev. d'orthop. **21**:323 (July) 1934.

Autopsy was performed on a child of 16½ months of age. The father was a cretin. The mother and two other children were healthy. There was no syphilis in the family. The child was born at term with a normal delivery. The abnormal observations at autopsy were as follows:

The frontal and parietal bones were widely separated and ragged. The scapulae were of normal size; the acromion was directed more posteriorly than normal; the glenoid fossa was small, and the lower rim was absent. (There was subluxation of the humerus below the glenoid.) The clavicles were rudimentary and attached to the sternum and acromion by fibrous bands. The arms were normal except for the phalanges, which were atrophic. The sternum did not show any evidence of fusion between its component parts. Examination of the pelvis showed that the pubic center was apparently absent. The phalanges of the toes were small.

The etiology of the condition is supposed to be an increased intra-uterine pressure, producing a partially diminished circulation to the rapidly growing structures. This increased pressure is supposed to occur at about the eighth week of intra-uterine life; consequently the tissues affected are those that have not reached complete development of form, such as the vault of the skull, the clavicles and the phalanges. The pubic bones do not appear until about the fourth month. Changes in these speak for dysostosis. According to Murk Jansen, the four characteristic changes are: (1) arrested development, (2) partial or complete loss of the clavicles, (3) small fingers and toes and (4) bilateral flattening of the thorax. The mystery of dysostosis is still to be solved. What produces the pressure is unknown.

RYAN, Vancouver, Canada.

OXYCEPHALIA AND ZONULAR CATARACT. AUBARET and GUILLOT, Rev. d'oto-neuro-opht. **12**:279 (April) 1934.

The patient had typical oxycephalia with poorly developed intellect. Defective vision was noted at the age of 12 years; vision was 1/10 in the right eye and 3/10 in the left eye. Examination revealed a double zonular cataract, synosteosis

of the cranial sutures and thickening of the walls of the skull. The interesting question is whether there is an etiologic relationship between the cranial malformation and the alteration of the crystalline lens. Recent studies of the pathogenesis of cataract have shown the influence of the endocrine glands in some cases, especially the important rôle of the parathyroids in cataract and in Paget's disease.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

CERTAIN CONGENITAL MALFORMATIONS OF THE HANDS AND FEET. A. ZUPPA, Pediatria **42**:943 (Aug. 1) 1934.

Twelve cases of congenital malformation of the hands and feet are described. Zuppa discusses each of these fully and illustrates each type by a roentgenogram. He suggests that roentgenography is absolutely essential for the proper diagnosis of this type of anomaly.

SIGNORELLI, New Orleans.

DYSTOCIA FROM AN ASCITIC FETUS. P. BRANDO, Rev. de gynec. e d'obst. **27**:181 (April) 1934.

The mother was 40 years old and had had twelve children, five of whom were living. There was no suspicion of syphilis. The fetus was contained in an immense sac estimated as holding 5.5 liters of fluid. Some of the common causes of fetal ascites are discussed.

SANFORD, Chicago.

Diseases of the New-Born

MENINGITIS IN THE NEWBORN. CARROLL POUNDERS, J. Pediat. **4**:752 (June) 1934.

A case of meningitis due to an unknown organism of the paracolon group, occurring in a 5 week old infant is reported. There had been a difficult labor followed by a suppurating wound of the scalp and possibly an intracranial injury. Among the factors predisposing to meningitis in a new-born infant may be mentioned the high permeability of the intestinal tract, the low degree of general immunity and the areas of low resistance caused by intracranial injuries. It is possible that many cases of meningitis in new-born infants are not recognized.

LEMASTER, Evanston, Ill.

VOMITING AND CONVULSIONS IN THE NEWBORN INFANT WITH SPECIAL REFERENCE TO TETANY. MURRAY H. BASS, M. Clin. North America **17**:1241 (March) 1934.

Convulsions occasionally occur in infants suffering from pyloric obstruction. Such patients as have been studied have not, however, presented the characteristic features of tetany, such as carpopedal spasm, Chvostek's sign, Trousseau's sign and hyperirritability to the electric current. The reasonable explanation of the cause of the convulsions in these cases is that they are due to alkalosis resulting from loss of chlorides. The treatment is the replacement of the lost chlorides, which is best accomplished by intravenous and subcutaneous infusions.

Convulsions of a different character, more closely resembling tetany, occur in other vomiting infants. Besides convulsions, these infants present a characteristic set of symptoms consisting of refusal of food, vomiting, high fever, distention and multiple convulsions. There are also present such peculiar symptoms of tetany as typical carpopedal spasm, laryngismus, Trousseau's sign and Chvostek's sign. While the blood calcium in these cases may be fairly high, the prompt cessation of symptoms in response to calcium therapy is so dramatic that there can be little doubt that they are symptoms of true tetany.

The recognition of these conditions by pediatricians and obstetricians is very important, since the prompt application of appropriate treatment is a veritable life-saving measure.

EUGENE SMITH, Ogden, Utah.

HYPERTONIC RECTAL SALINE FOR INTRACRANIAL INJURY IN THE NEWBORN. ALAN MONCRIEFF, Brit. M. J. **1**:1068 (June 16) 1934.

In the opinion of Moncrieff, many cases in which symptoms of intracranial injury occur are those of edema rather than hemorrhage. Of course, the occurrence of hemorrhage is not denied. Edema can account for all the symptoms. The author thinks that many of these symptoms can be speedily relieved by the introduction of from 2 to 3 ounces (59.14 to 88.7 cc.) of a 10 per cent saline solution into the rectum of the newly born as soon as symptoms appear. His experience in a number of cases has made him feel that it is advisable to use the same procedure as a prophylactic measure. The rectal administration is repeated when it is deemed advisable as often as every four to six hours. His experience with this method has made him conclude that it is very valuable.

ROYSTER, University, Va.

ICTERUS GRAVIS NEONATORUM. W. R. F. COLLIS, Irish J. M. Sc., March, 1934, p. 106.

Collis describes a case of this condition with recovery. The child had the usual family history. Treatment consisted of four transfusions and twenty-two injections of human serum. The transfusion from the mother seemed to be the most efficacious.

SNELLING, Toronto, Canada.

A CASE OF CARBUNCLE SEPTICEMIA; TRANSPLACENTAL TRANSMISSION. R. ISMAEL MENA, Arch. chil. de morfol. **1**:39, 1933.

A pregnant mother, 36 years of age, had a carbuncle on the right side of her mouth, with swelling of the face and neck. Eleven days later her baby was born, and it died within three hours. At autopsy the spleen was found to be hyperplastic, with deposits of pigment and a hemorrhagic pulp. By the Gram-Weigert stain the splenic sections revealed many bacteria (called by the author bacteria of Davaine).

HERRON, Spokane, Wash.

ANATOMY OF THE NEW-BORN. ERNA MAHN HECKER, Arch. chil. de morfol. **1**: 59, 1933.

This is an excellent treatise on the anatomy of the new-born. It is divided into three major sections. The first deals with all the abdominal viscera, and the second with the gastro-intestinal tract alone. The peritoneum forms the subject matter of the third section, which is followed by an appendix on the subject of situs inversus viscerum. The embryology, anatomic location, fixation, blood supply, size, shape and various anomalies of each organ are discussed in detail. It would be well worth while to have an exact translation into English.

HERRON, Spokane, Wash.

NEONATAL MORTALITY IN SALVADOR, BAHIA, 1923 TO 1932. ALVARO DA FRANCA ROCHA, Pediat. e puercultura **3**:229 (Dec.) 1933.

The neonatal mortality for the capital of Bahia was 119.95 per thousand of registered births and 68.79 per thousand of the probable births for the years 1923 to 1932. The mortality depended on medical, hygienic and social conditions. Syphilis caused the greatest number of deaths, with obstetric causes next.

SANFORD, Chicago.

Acute Infections

THE TRANSMISSION OF DIPHTHERIA ANTITOXIN FROM HEN TO EGG. T. H. JUKES, D. T. FRASER and M. D. ORR, J. Immunol. **26**:353 (May) 1934.

A series of hens were immunized with diphtheria toxoid. A large amount of toxoid (as much as 52 cc.) was required to produce a definite but low concen-

tration of antitoxin in the serum. Antitoxin was demonstrated in the eggs in amounts that seemed to bear some relationship to the concentration in the blood serum. The various proteins in the eggs were separated, and the bulk of the antitoxin was associated with the livetin fraction of egg yolk.

FOTHERGILL, Boston.

ON THE USE OF IMMUNE SERUM AT VARIOUS INTERVALS AFTER THE INOCULATION OF YELLOW FEVER VIRUS INTO RHESUS MONKEYS. N. C. DAVIS, J. Immunol. **26**:361 (May) 1934.

Immune serum from animals which had recovered from yellow fever prevented or ameliorated symptoms in a significant number of monkeys if it was given from twenty-four to forty-eight hours after the injection of yellow fever virus. If the injection of immune serum was delayed until a temperature of 104 F. first developed there was no effect whatever on the course of the disease.

FOTHERGILL, Boston.

IMMUNOLOGIC STUDIES IN A CASE OF TYPHOID WITH RELAPSES. G. D. C. THOMPSON and E. E. ECKER, J. Infect. Dis. **54**:177 (March-April) 1934.

Thompson and Ecker report the case of a patient who had three attacks of typhoid fever within three months. Precipitins and agglutinins were lacking, although there were a positive complement-fixation reaction, bacteriolytic antibodies and marked opsonic powers.

TOOMEY, Cleveland.

OBSERVATIONS ON THERAPY IN ERYSIPELAS. PHILLIP E. ROTHMAN, J. Pediat. **4**: 746 (June) 1934.

Reports on the use of antitoxin, blood transfusions, roentgen therapy and local measures in erysipelas in infants and children are analyzed and discussed. It is shown that a great many of these reports are based on inadequately controlled series or without due significance to the age of the patients. More carefully analyzed reports are necessary before any final conclusions can be made.

LEMASTER, Evanston, Ill.

THE VALUE OF HUMAN BLOOD SERUM IN SEPTICEMIA. P. LAZARUS-BARLOW and L. P. BLANEY CHAMBERLAIN, Lancet **1**:503 (March 10) 1934.

Having observed that in cases of septicemia in which antiserums failed, small transfusions often brought about improvement, the authors adopted the following procedure: A patient, whose condition was diagnosed as septicemia or sapremia was given an intramuscular injection of antiserum. If no improvement took place within twenty-four hours, as indicated by a fall in the temperature and pulse rate, an injection of fresh human serum was given. If further antiserum was considered necessary, it was almost always given alone and was followed by an injection of human serum twenty-four hours later. This procedure was adopted on the hypothesis that some patients lack complement and thus are unable to utilize the antibodies in the antiserum. Of twelve patients, ten, who had not responded to the administration of the antiserum, showed improvement, which was marked in some cases, after the administration of the human serum.

LANGMANN, New York.

THE BLOOD-BRAIN BARRIER IN INFECTIOUS DISEASES. U. FRIEDEMANN and A. ELKELES, Lancet **1**:734 (April 7); 775 (April 14) 1934.

Friedemann and Elkeles believe the most important result of their studies to be the demonstration that the blood-brain barrier plays an important and hitherto overlooked part in the pathogenesis of infectious diseases. From a reconsideration of the literature and from studies of their own they have arrived at the con-

clusion that this barrier is impermeable to some toxins, e. g., diphtheria and botulinus toxin, which were hitherto generally supposed to owe their lethal effects to their actions on the brain. Further, it could be shown that toxins differ among themselves in their ability to pass the blood-brain barrier. From this point of view toxins fall into two distinct groups: one, containing lamb dysentery toxin and cobra venom, passes the blood-brain barrier, whereas the other, containing tetanus, diphtheria and botulinus toxins, does not pass it. The toxins fall into the same groups when arranged according to their electrical charges. Diphtheria, tetanus and botulinus toxins carry a negative charge at the p_H of the blood; lamb dysentery toxin is neutral, and cobra venom carries a positive charge. It would thus appear that a negative charge inhibits permeation through the brain-blood barrier.

LANGMANN, New York.

GLANDULAR FEVER AND INFECTIOUS MONONUCLEOSIS. H. LETHEBY TIDY, Lancet **2**:180 (July 28); 236 (Aug. 4) 1934.

Tidy comes to the following conclusions:

1. Glandular fever is an acute infectious disease characterized by fever, grandular enlargement and changes in the blood (especially mononuclear), and sometimes by severe faucial changes. No person of any age is immune, but children are most liable to the infection.

2. Three principal types can be recognized: (*a*) the glandular, or Pfeiffer's, type, (*b*) the anginose type (monocytic angina) and (*c*) the febrile type.

3. Suppuration of the glands is rare.

4. Eruptions are common in the febrile type and its variations. There are usually maculopapular, resembling the eruption in typhoid fever and rubelliform eruption, especially in children.

5. All the blood-forming tissues are affected. The myeloid tissues tend to react more rapidly, producing initial transient polynucleosis or neutropenia. The lymphoid tissues react more slowly, producing mononucleosis. The total number of leukocytes rarely exceeds 40,000 per cubic millimeter, but may reach 60,000 in young children.

6. The mononuclear cells are increased both relatively and absolutely. Numerous types of abnormal mononuclear cells tend to be present simultaneously. The abnormal cells may represent any or every type, from lymphocytes to plasma cells (monocytes). The predominant cell may vary in different cases and may alter in type in the course of an individual case.

7. The prognosis is favorable, and the mortality in healthy subjects is negligible.

8. The virus is unknown but is probably transmissible to monkeys.

LANGMANN, New York.

PROPHYLAXIS OF SCARLET FEVER. H. KLEINSCHMIDT, Bull. Assoc. internat. de pédiat. prevent. **1**:16 (Sept.) 1934.

Isolation of patients with scarlatina frequently prevents the spread of the disease. On the other hand, fresh cases have been met with in spite of passive serum immunization. Even after treatment by serotherapy no prophylactic effect has been observed that prevents complications of a toxic nature; indeed, one meets with relapses, sometimes at an early date. Diphtheria serum and scarlatina serum are as little comparable in their effects as are diphtheria toxin and the filtrates of cultures of Streptococcus.

Active protective vaccination against the scarlatina streptococcus by means of an ointment containing diphtheroid toxoid and dead diphtheria bacilli does not give satisfactory results. The absence of the hemolytic streptococcus is not a sufficient safeguard against recurrence. On the other hand, serotherapy has reduced the percentage of recurrence from 7.9 to 4.7. The hypothesis according to

which the hemolytic streptococcus is the cause of scarlatina is founded primarily on the fact that in cases of traumatic scarlatina the bacillus has almost always been found in the wound. However, it is well to remember the observations made in the case of swine fever, in which Bacillus suipestifer played a secondary rôle only, the real agent being a filtrable virus.

AMESSE, Denver.

THE SCHICK REACTION IN TESTING IMMUNITY TO DIPHTHERIA IN THE BLACK RACE OF SOUTH AFRICA. E. GRASSET and A. PERRET-GENTIL, Compt. rend. Soc. de biol. **113**:1457 (July 22) 1933.

The following tabulation is a summation of the Schick test on persons in South Africa. Details of the climatic points may be found in the original article.

Age	Total Tested	No. Positive Schick Reactions	Positive Reactions, Percentage
4 months-3 years	17	8	47.05
4-6 years	27	9	33.33
7-10 years	66	6	9.09
11-20 years	179	8	4.47
21-40 years	224	14	6.25
Over 40 years	54	2	3.71

The average number of positive reactions for the entire group was 8 per cent. The interpretation follows that the percentage of positive reactions for a given age is similar to that in European countries, but the ratio is considerably smaller, owing to greater acquired immunity.

WAHL, Cleveland.

NATURE OF THE IMMUNITY TO DIPHTHERIA IN THE BLACK RACE; DETERMINATION OF THE ANTITOXIN IN THE BLOOD. E. GRASSET and A. PERRET-GENTIL, Compt. rend. Soc. de biol. **113**:1461 (July 22) 1933.

The following tabulation shows the results obtained for subjects in different sectors of South Africa:

Antitoxin, units	>1	>½	>⅕	>1/10	>1/25	>1/50	<1/50	Total
No. of subjects	4	5	67	36	33	14	13	172
Percentage	2.3	2.9	38.9	20.9	19	8	7.5	

It is seen that 7.5 per cent have less than 1/50 unit of antitoxin per cubic centimeter of blood, and this coincides with the 8 per cent of persons with positive Schick reactions as determined previously. This only substantiates further the relatively greater immunity of the black race of South Africa against diphtheria.

WAHL, Cleveland.

HEMATOLOGIC MODIFICATIONS IN MEASLES. G. STANCANELLI, Pediatria **42**:457 (May 1) 1934.

Nine cases of measles in young infants were studied by Stancanelli. His observations showed constant functional variations in relation to the hematopoietic organs, which were moderate during the incubation period but increased appreciably during the prodromic period and reached their height during the eruptive stage. In cases in which complications developed these functional variations continued throughout the complications. The author summarizes his findings to include a diminution of the hemoglobin and a decrease in the total red and white cell count, followed by a gradual increase in the white cell count. Frequently leukocytosis was found during the course of complications. During the prodromal period there were present considerable numbers of myelocytes and metamyelocytes. Arneth's scheme showed a shifting to the left during the prodromal period and the eruptive period and also during the existence of complications in cases in which these developed.

SIGNORELLI, New Orleans.

DIAGNOSTIC CONSIDERATIONS IN A CASE OF SPORADIC AND ATYPICAL GLANDULAR FEVER. WILLY SCHWARZ, Pediatria **42**:498 (May 1) 1934.

A case is reported in which the principal features were fever, a slight and transitory swelling of the superficial lymph nodes, enlargement of the spleen and liver and marked hyperleukocytosis (a total white count of 160,000), with lymphomonocytosis (93 per cent). From the latest description of Pfeiffer's glandular fever of the leukemic type Schwarz believes his case to belong to this group. His patient died of intercurrent disease. The autopsy, while excluding lymphatic leukemia, showed one of the few anatomic observations in glandular fever. Schwarz believes that, contrary opinions notwithstanding, glandular fever is a definite infectious disease which cannot be easily differentiated clinically from leukemia.

SIGNORELLI, New Orleans.

OCCURRENCE OF DIPHTHERIA IN FAMILIES. LUISE HOLL, Monatschr. f. Kinderh. **60**:264, 1934.

In a two year study in which 930 individual cases of diphtheria were recorded, 255 siblings of the affected children contracted the disease in 110 families. Of these 255, only 80 showed symptoms during the first six days of the first illness in the family. The majority sickened only weeks or months later. Only 16 were affected during the third to the twelfth day after the return of a convalescent. Severe toxic cases rarely occurred twice in the same family.

Holl offers these interesting statistics in favor of the idea that diphtheria is not highly contagious, but that susceptibility is a matter of individual and familial constitution.

GERSTLEY, Chicago.

AN EXPLANATION OF IMMUNITY TO DIPHTHERIA. F. H. LORENTZ, München. med. Wchnschr. **80**:1388 (Sept. 8) 1933.

In a paper entitled "Nutrition and Mortality" Hahn concluded that (1) every vitamin deficiency decreases immunity and (2) in the spring there is a deficiency in the dietary of Germans. Lorentz thinks that these conclusions have not been adequately applied in the prophylaxis and treatment of diphtheria. He has found considerable data in the literature to support his view that immunity to diphtheria is closely related to the vitamins, whether these are obtained from food or sunlight. Wells, and Wells and Heinbecker found that the Eskimos have an unusually high titer of diphtheria antitoxin in their blood and that diphtheria among them is uncommon. According to Lorentz, this is due to the consumption of large quantities of fish and cod liver oil. Otto Fischer examined a group of Negroes between 7 and 22 years of age in East Africa. Only three of two hundred and eighty-three gave positive Schick reactions. Of those who gave negative Schick reactions 27 per cent had either less than $\frac{1}{20}$ unit of antitoxin or none. According to Lorentz, this means that persons highly vitaminized, so to speak, by sunlight or diet require only a minimal amount of antitoxin to neutralize toxin or that they are able to produce antitoxin faster and better when it is needed. A similar conclusion can be drawn from the observations of Asbelew and Margo, who examined the natives of Samoa. Neither diphtheria nor scarlet fever occurs there, but all the natives tested gave negative reactions to the Dick and Schick tests. The beneficial effects of treatment of diphtheria with antitoxin or normal horse serum may be due to the vitamins present in the serum. The vitamins stimulate the production and mobilization of immune bodies.

BRAHDY, Mount Vernon, N. Y.

AN EPIDEMIC OF SPASMODIC COUGH SIMILAR TO WHOOPING COUGH. H. PÄSSLER, München. med. Wchnschr. **81**:511 (April 6) 1934.

Pässler describes an outbreak of spasmodic cough in adults many of whom had had whooping cough. The condition is contagious, may have a short incubation period and begins with an alteration in the sense of taste and tracheitis lasting a

week or two and followed by typical spells of spasmodic cough which may persist for several months. There is no tendency to vomit. Complications are uncommon. Many drugs were tried to alleviate the symptoms, but the only one which was beneficial was quinine given in repeated doses of 0.1 Gm.

BRAHDY, Mount Vernon, N. Y.

DESTRUCTION OF VACCINIA VIRUS BY LIGHT ENERGY AND DYES. K. HERZBERG, Ztschr. f. Immunitätsforsch. u. exper. Therap. **80**:507, 1933.

The virucidal effect of various dyes, notably methylthionine chloride, U. S. P. (methylene blue), was greatly enhanced by combination with light, particularly with ultraviolet rays. Different experimental conditions and results are described and evaluated.

DAVIDSOHN, Chicago. [ARCH. PATH.]

OHARA'S BACILLUS IN DYSENTERY: AGGLUTINATION TEST ON OHARA'S BACILLUS IN CHILDREN IN MUKDEN ATTACKED BY DYSENTERY AND LIKE DISEASES. MATSUJI KITAMURA and MASAU ENDO, J. Orient. Med. **19**:74 (Nov.) 1933.

Agglutination tests with the serum of thirty-seven healthy Mukden children and Ohara's bacillus (Bacillus paradysenteriae Sonne III) showed 1:80 to be the highest dilution in which agglutination occurred. In seventeen of ninety-seven children with diarrhea the agglutination test was positive with dilutions of 1:160 or higher. Ohara's bacillus was cultured from the stools of four patients.

LEMASTER, Evanston, Ill.

TWO CASES OF ICTERO-HEMORRHAGIC SPIROCHETOSIS IN CHILDHOOD. I. KOBAYASHI, J. Pediat. (Tokyo), Nov. 20, 1933, no. 402, p. 2025.

Icterohemorrhagic spirochetosis is extremely rare in childhood. In the two cases reported in this article there was a sudden onset, with malaise, pains in the limbs and marked anorexia. Hemorrhages and petechiae were noted in one case, but not in the other. Jaundice appeared on the fourth and sixth day respectively, and the Meulengracht test showed 25 and 34, respectively. No splenomegaly was present. There was evidence of nephritis. The neutrophils were increased, and the eosinophils and lymphocytes were decreased, as were the platelets. Spirochaeta icterohaemorrhagiae was demonstrated in both cases.

KATO, Chicago.

DIPHTHERIA CARRIERS AND THEIR TREATMENT. ALBIN LANDAU, Acta pædiat. **15**:211 (March 28) 1934.

Landau defines as primary carriers persons who harbor diphtheria bacilli in their upper respiratory tract despite the fact that they cannot be shown to have had the disease previously. Secondary carriers are those in whom the organism persists after an attack of clinical diphtheria. Bearing in mind the possible mildness of diphtheria, it is probable that most carriers are secondary.

The infectiousness of patients after diphtheria is variable; hence the exact definition of the carrier state is somewhat arbitrary. As a corollary, the exact number of negative cultures necessary for discharge from contagious isolation and the time that should elapse between each culture depend on individual experience. Weaver studied five hundred consecutive cases of diphtheria, with the following results:

From the onset of the disease 71.2 per cent of the patients showed three negative cultures in three weeks, and 83.2 per cent showed three negative cultures in four weeks. Less than 1 per cent required seven weeks to conform with this criterion. After eleven weeks only one patient harbored bacilli. Tonsillectomy was performed on some of these patients before they were released from isolation. Landau's experience with the same number of patients was in agreement with Weaver's results. He emphasizes the well known fact that the technic of taking cultures has an important influence on the result of the test. The duration of

quarantine is determined by the number of negative cultures demanded before release. Hartley and Martin found that the mean period of isolation for patients discharged after one negative culture was twenty-one days; after two negative tests, thirty-four days, and after three negative tests, forty-five days. Frequently a person may harbor the Klebs-Löffler bacillus for many months, giving rise to contact cases during the entire period. Rarely, chronic infection of the carrier may be present with persistent clinical symptoms.

Innumerable methods have been employed to curtail the carrier stage and make it possible to return the patient more quickly to society. Alternately encouraging and disappointing experience has been reported with gargles of boric, citric and hydrochloric acid, mercuric chloride, potassium iodide, sulphur dioxide, quinine, sodium bicarbonate, menthol, hydrogen peroxide, malonic acid and other preparations. The following remedies have been used internally: arsenic, potassium iodide, turpentine, mercury cyanate, formaldehyde and others. Silver nitrate, tincture of iodine, sodium diiodoparaphenolsulphonate and the enzyme that occurs with pyocyanase have been employed for topical application. Inhalations of thymol have been recommended. Some authors have reported good results with strong silver protein, mercurial ointment, iso-amylhydrocupreine, tribromonaphthol and gentian violet. Schiötz advises that the throats of carriers be sprayed with pyogenic cocci. The use of "detoxicated Klebs-Löffler vaccine," ultraviolet light and the roentgen rays has been described.

Landau believes that the multiplicity of proposed agents argues against the efficacy of any single one. He accepts as a fundamental premise that carriers exhibit pathologic alterations of the lymphoid tissue of the pharynx and nasopharynx. Those who harbor the organism in the throat are decisively benefited by tonsillectomy, whereas repeated nasal irrigation is an efficacious measure for those who carry the organism in their nasal passages. He regards the surgical principles of eradication of foci and adequate drainage to be of greater importance than attempts at chemical sterilization or specific immunologic treatment with antitoxin. Numerous reports of cases are adduced to illustrate and prove this contention.

McCune, New York.

Chronic Infections

Certain Aspects of Pulmonary Tuberculosis in Children. Roy Morgan, Am. Rev. Tuberc. **29**:577 (May) 1934.

During a period of twenty-two years, six hundred and thirty-one children and adolescents (under 18 years of age) with pulmonary tuberculosis of the adult type have been under observation. The mortality in this series has been discouragingly high, owing partly to the advanced stage at which many of the patients were admitted and partly, it may be, to the fact that strict rest in bed was not insisted on prior to 1920. However, Morgan is convinced that moderately advanced and advanced pulmonary tuberculosis in children and young adults is an extremely serious disease. The vast majority of these patients will be lost, even if given prolonged treatment in bed. During the past two years artificial pneumothorax has been used in suitable cases. This procedure offers hopes of improving results, but not to such an extent as to greatly change the figures for the mortality. In incipient cases, rest in bed seems to produce good results. It is necessary, however, to discover the disease while it is early and curable.

Eugene Smith, Ogden, Utah.

Syphilis and the General Practitioner. N. O. Eaddy, J. South Carolina M. A. **30**:127 (June) 1934.

Eaddy lives in a community which will give the cross-section of the number of persons with positive syphilitic reactions in the rural territories of South Carolina. Wassermann tests for syphilis were done on one hundred and sixty-two patients.

There were 17 per cent positive reactions for white males as opposed to 10.5 per cent for white females and 23 per cent positive reactions for Negro males as opposed to 44 per cent positive reactions for Negro females. Twenty-nine white males and nineteen white females and sixty-four Negro males and fifty Negro females were examined. The relatively high percentage of Negro females is called to the reader's attention. Eaddy concludes by urging every general practitioner to do a Wassermann test on every patient. WESTON JR., Columbia, S. C.

THE CHILDHOOD TYPE OF TUBERCULOSIS. LEONARD G. PARSONS, Lancet **1**:1101 (May 26) 1934.

This is an excellent review of the present knowledge of the childhood type of tuberculosis. The present understanding of the primary complex is clearly defined, and Parsons emphasizes the view that the actual result of the primary infection of the lungs depends almost certainly on the size of the infecting dose. He agrees with Spence that the whole lesion in epituberculosis should be regarded as a benign form of tuberculosis and not a pure allergic reaction. To substantiate this view he cites numerous instances in which tubercle bacilli were recovered on needling the epituberculous pulmonary area.

A word of caution is added in regard to taking too optimistic a view of these benign infections. The menace of tuberculous meningitis is emphasized.

In 671 children under 12 years of age who were examined post mortem at the Children's Hospital, Birmingham, during a period of twenty-one months death was caused by tuberculosis, chiefly tuberculous meningitis, in 100 instances. In 71 cases a particularly painstaking search was made for Ghon's tubercle, and this was present in 49. LANGMANN, New York.

BACILLIFEROUS SPUTUM IN OLDER CHILDREN WITHOUT CONSTITUTIONAL DISTURBANCE. F. FAURE and MATINIER, Presse méd. **42**:848 (May 23) 1934.

Faure and Matinier report three cases of children of 13, 14 and 16 years, respectively, all of whom were directly exposed to active tuberculosis and who showed no clinical or roentgen evidence of the disease. All three had sputum positive for tubercle bacilli. The children developed normally. The authors discuss the possible explanations for the presence of the bacilli, among these being the existence of the organism as a saprophyte in the respiratory tract, the migration of the bacilli from lesions hitherto encysted and the possibility that the patients are carriers of the bacillus. The last explanation is the most plausible.

BIEKER, St. Petersburg, Fla.

ALLERGIC PROPERTIES OF B C G VACCINE. R. TURPIN, Progrès méd., no. 26, June 30, 1934, p. 1081.

A systematic study and comparison of the cutaneous reactions to tuberculosis in children vaccinated with B C G, both in those in the best of surroundings and in those exposed to tuberculosis, shows that those exposed to tuberculosis have a high resistance. A strong and durable allergic reaction is the only apparent sign of this reinfection. SANFORD, Chicago.

SOME RECENT STUDIES ON B C G. HENRI SCHWERS, Progrès méd., no. 26, June 30, 1934, p. 1086.

Schwers reviews the literature in France for the last year on B C G. From a clinical standpoint the report of Sotty in the *Bulletin de l'Académie de médecine de Paris* on an eight year study of the results of vaccination in children and from a bacteriologic standpoint that of Nègre in the same journal are of interest. Needless to say, the reports are highly favorable. SANFORD, Chicago.

THE FIRST INFANT VACCINATED WITH B C G IN RIO DE JANEIRO. ALVIMAR DE CARVALHO, Arch. de pediat., Rio de Janeiro **6**:691 (April) 1934.

The first infant vaccinated with B C G by the Liga Brasileira contra Tuberculose was 7 years of age on Aug. 28, 1934. The mother died of tuberculosis in January 1930. He had been in contact with her first for fifteen days following birth and second for a period of five months during the active stage of her disease. Roentgenograms of the child and skin tests showed that the disease had entered his body but made no headway. The author has gone into detail in this case to show the efficacy of vaccination against tuberculosis.

SANFORD, Chicago.

ERYTHEMA NODOSUM AND TUBERCULOSIS. PASCUAL R. CERVINI and GUILLERMO A. BOGANI, Arch. argent. de pediat. **4**:660 (Sept.) 1933.

The authors report fourteen cases of erythema nodosum in children ranging in age from 2 to 12 years. All the patients showed definite evidence of tuberculous infection, mostly pulmonary lesions. Biopsy of a nodule was performed in one case and the tubercle bacillus demonstrated in the lesion. SCHLUTZ, Chicago.

MILIARY TUBERCULOSIS IN THE CHILD. R. LUIS CID, Arch. de Hosp. d. niños **4**:87 (Dec.) 1933.

The miliary form of tuberculosis generally appears in attenuated form in the child. According to the author, the disorder can be divided into three stages: the acute, subacute and chronic.

In the acute stage, symptoms resembling a typhoid or a meningeal state predominate. In the infant the disorder may simulate the syndrome seen in alimentary intoxications. In the chronic forms the picture is more atypical. Miliary tuberculosis is not often seen in the child. If it does occur it is hematogenous in origin.

In the majority of both acute and chronic cases, roentgen examination will establish the diagnosis. If roentgen examination definitely indicates miliary tuberculosis, it is well to look for tuberculous lesions in the choroid coat of the eye.

It is difficult to classify miliary tuberculous nodules. Grossly, three types may be distinguished: actively enlarging nodules, mixed forms and those tending to caseation. From the histologic structure of the nodule, it is possible to estimate the gravity of the miliary process and its probable duration.

In the acute forms of three or four weeks' duration there is tendency to caseous pneumonia. In cases extending beyond seven weeks there is some tendency to fibrosis. In miliary tuberculosis, the primary lesion is in the alveoli, and the nodules form in the acini. In most of the nodules elastic fibers can be demonstrated.

In this type of the disease there is an excellent opportunity to study the histogenesis of tuberculosis in all its gradations and forms. SCHLUTZ, Chicago.

VACCINATION WITH B C G. ARLINDO DE ASSIS, Movimento pediat. **1**:70 (April) 1934.

The entire subject of vaccination with B C G was reviewed by the author in honor of the memory of Professor Calmette, at the Sociedad Brasileira de Tuberculose.

SANFORD, Chicago.

INTELLIGENCE TESTS IN CHILDREN WITH CONGENITAL SYPHILIS. PAUL VON KISS and TIBOR RAJKA, Arch. f. Kinderh. **102**:25 (April 27) 1934.

Forty-five children with congenital syphilis were subjected to the Binet-Simon intelligence tests. Intelligence was below normal in 37.8 per cent. The age at which treatment was begun was found to make a great difference. Whereas 58.8 per cent of the children who were not treated until they were over 2 years old showed a subnormal intelligence, only 9 per cent of those treated from the first

year of life were mentally retarded. Obviously every effort should be made to furnish antisyphilitic treatment to the children of syphilitic parents from earliest infancy.

LeMaster, Evanston, Ill.

Diagnosis of Experimental Tuberculosis with the Ninni Technic. Vladimir Mikulowski, Monatschr. f. Kinderh. **60**:292, 1934.

The ordinary method of diagnosing tuberculosis by the inoculation of guinea-pigs requires from five to six weeks. The Ninni technic consists of surgically exposing the cervical lymph nodes of the guinea-pig and injecting 0.1 cc. of the suspected material into each of the isolated nodes. The diagnosis can then be made in from ten to twenty days. Mikulowski used this method in testing thirty spinal fluids and twenty exudates and sputums and found it very satisfactory. In the cases of tuberculosis the lymph nodes became palpable within two weeks.

Gerstley, Chicago.

Subacute and Chronic Cervical Lymphadenitis as a Diagnostic Sign of Primary Tonsillar Tuberculosis. E. Schlittler, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:400 (April 6) 1934.

A review of the cases of primary tonsillar tuberculosis confirmed by necropsy shows that a swelling of the lymph nodes draining the tonsils occurs in the neighborhood of the angle of the jaw. Schlittler reports that in ninety-eight cases in which the patients had chronic or subacute lymphadenitis at the angle of the jaw definite microscopic tuberculosis was demonstrated in the removed tonsils forty-eight times. Primary tonsillar tuberculosis is therefore the diagnosis of choice in the presence of this type of adenopathy. In these forty-eight cases of histologically proved tonsillar tuberculosis, a pharyngeal tonsil was the seat of the lesion seven times, a pharyngeal and a palatine tonsil six times, both palatine tonsils seven times, and one palatine tonsil twenty-eight times. Several features of the condition in these forty-eight cases speak for the primary involvement of the tonsil: the absence of open pulmonary tuberculosis or tuberculosis of other organs; the further behavior of the patients after removal of the tonsils; the strict localization of enlarged lymph nodes to the region draining the tonsils, and finally the relative frequency of involvement of only one tonsil (73 per cent). The author believes that in the rest of the ninety-eight cases, in which no tuberculous changes were found in the tonsils, the primary factor might still be tuberculous, but the condition had healed to such an extent that the original lesion was not found. He finds evidence for this view in the decreasing number of cases of this type in which he and his associates are unable to find tuberculosis of the tonsil after removal.

Editor's Abstract. [Arch. Otolaryng.].

Internal Diseases

Amebiasis and Amebic Dysentery. Charles F. Craig, Am. J. Digest. Dis. **1**:4 (March) 1934.

This is a complete and excellent article, the essential points of which may be summed up as follows: 1. Amebiasis, with symptoms that may vary from slight digestive disturbances to the most severe symptoms of amebic dysentery or amebic abscess of the liver or other organs, occurs in from 5 to 10 per cent of the population of this country. 2. By amebic dysentery is meant a symptom complex characterized by a bloody mucoid diarrhea, caused by Endamoeba histolytica and occurring as one of the clinical manifestations of amebiasis. 3. This condition may be transmitted by (*a*) a polluted water supply; (*b*) the use of human excreta in the fertilization of garden vegetables; (*c*) the droppings of flies, and (*d*) the handling of food by infected persons who are excreting the cysts

of the parasites in their feces. 4. As the symptoms and physical signs may, of necessity, vary greatly, the diagnosis must always depend on the presence of Endamoeba histolytica in the stools or scrapings of the ulcers. 5. The prophylaxis depends entirely on the prevention of the contamination of food and drink, and examination of food handlers should be carried out as a routine measure. 6. Craig believes that the only value of emetine is to control the symptoms of dysentery. Acetarsone should never be used, because of its toxicity. Craig advocates the use of chiniofon, carbarsone, a bismuth tartrate preparation and vioform.

MORRISON, Savannah, Ga.

THE METABOLISM OF FEVER, WITH SPECIAL REFERENCE TO DIABETIC HYPERPYREXIA. HAROLD HINWICH, Bull. New York Acad. Med. **10**: 16 (Jan.) 1934.

All physiologic processes are accompanied by heat production. Loss of heat occurs through radiation and conduction from the skin and through evaporation from the skin (perspiration) and lungs. In the healthy person heat production and heat dissipation are a balanced mechanism, so that the body temperature remains close to 98.6 F., or 37 C. Any uncompensated change in this physiologic mechanism constitutes a pathologic reaction designated as fever. Fever may be due to insufficient loss of heat with a normal rate of production, or it may be the result of rapid oxidative processes due to toxic or infectious agents. (A malarial chill is accompanied by a rise in temperature of 3.5 C. [38.3 F.], but in a normal person in whom the paroxysm is imitated to the same extent of heat production there is a rise of only 0.5 C. [32.9 F.], because elimination of heat was correspondingly increased.)

Fever is classified under three headings: (1) that occurring in the presence of a normal mechanism for the production and elimination of heat in which the elimination cannot cope with the formation either because the production is too rapid (due to diathermy or extreme hyperthyroidism) or because the environment is too hot or too humid to permit adequate loss of heat (sunstroke); (2) that due to the pathologic conservation of heat in most infectious processes, and (3) that in which loss of heat is reduced due to anhydremia, in which there is a reduction in the body fluids and the skin is cold and dry.

In diabetes there is an alteration in water metabolism, as indicated by the symptoms of polydypsia and polyuria. Hyperpyrexia is easily produced in the diabetic subject by withholding water, depending on the high blood sugar content and diuresis to create an anhydremic condition with elevation of temperature (due to insufficient loss of heat). This phenomenon may be explained on the basis of increased specific gravity and osmotic pressure of the blood serum. As water leaves the blood there is an increased number of red blood cells per unit volume, with a consequent rise in oxygen capacity (hemoglobin). Experiments also show that in anhydremia the blood fluids are preserved for vital functions in the body, with reflex closure of the cutaneous blood vessels, thus causing inadequate loss of heat through the skin and hence the hyperpyrexia associated with anhydremia. Hyperpyrexia of this type may be successfully treated by the intravenous and oral administration of fluids.

JAHR, Omaha.

METABOLISM IN HYPERTHYROIDISM AND HYPOTHYROIDISM. WALTER WALKER PALMER, Bull. New York Acad. Med. **10**:52 (Feb.) 1934.

The discussion of the normal activities of the thyroid gland and its influence on metabolism is followed by a clinical dissertation on the disturbances in function of this gland: thyroid insufficiency and hyperthyroidism and its effects, particularly on the heart. Laboratory tests are stressed as valuable aids in diagnosis and treatment only on careful evaluation of findings. A laboratory test represents "a single component of a complicated system of dependent variables."

JAHR, Omaha.

STOMATITIS MEDICAMENTOSUS. SIGMUND S. GREENBAUM, Dental Cosmos **76**:353, 1934.

This is a concise article dealing with the symptoms, diagnosis and treatment of common oral lesions caused by ingested or locally applied drugs. The following groups are considered: (1) acetanilid, (2) antisyphilitic drugs, (3) barbital, (4) cinchophen, (5) gold compounds, (6) halogens, (7) phenolphthalein and (8) salicylates.

NOYES, Chicago.

CAUSES OF OBSCURE FEVERS IN INFANCY AND CHILDHOOD. CHARLES SCHOTT, Illinois M. J. **64**:485 (Nov.) 1933.

In order to emphasize that with careful examination and watchfulness an honest diagnosis may usually be made, Schott cites several cases in which the etiology was at first obscure. The causes in the cases cited were found to be Klebs-Löffler bacilli, pyuria, dehydration, pharyngitis, blebs on the ear drums, tracheitis, pneumonia, post-tonsillar infection, abscess of the brain, tuberculosis, leukemia, anaphylaxis, osteomyelitis and erythema subitum.

BARBOUR, Peoria, Ill.

THE DIAGNOSIS AND TREATMENT OF ANEMIAS IN INFANCY. ARTHUR F. ABT, Illinois M. J. **64**:572 (Dec.) 1933.

Following a review of the normal values for hemoglobin and red cells in the new-born and infants and a discussion of the physiology of the blood during fetal and early postnatal life, Abt discusses the following: anemia of the new-born, erythroblastosis in icterus gravis neonatorum, infectious anemias, infectious alimentary anemia, alimentary anemia, von Jaksch's anemia and erythroblastic anemia of Cooley and the treatment of the anemias of infants. He points out that whether the mechanism is infection, with destruction of blood and toxic suppression of the bone marrow, or omission of blood materials from the diet in nutritional anemia, the general form of treatment is the same.

BARBOUR, Peoria, Ill.

OVARIAN THERAPY. RELATIONSHIP OF THE FEMALE SEX HORMONE TO HEMOPHILIA. J. BREM and J. S. LEOPOLD, J. A. M. A. **102**:200 (Jan. 20) 1934.

Several favorable reports on the use of ovarian extract in the treatment of hemophilia led to the theory of the close relationship of the female sex hormone to hemophilia. The results of the investigations by Brem and Leopold do not support this theory. They were unable to demonstrate the presence of the estrogenic substance in the urine of normal males, and the commercial estrogenic substances employed by them failed to reduce the coagulation time of the blood or stop several hemorrhages in a hemophiliac. They believe that symptomatic treatment and blood transfusions are the methods of choice at present.

BONAR, Salt Lake City.

ARGYRIA: REPORT OF TWO CASES IN CHILDREN. H. K. BERKLEY, J. A. M. A. **102**:202 (Jan. 20) 1934.

The intranasal use of colloidal silver preparations for infections of the upper respiratory tract in children has enjoyed rather widespread use. Many times the preparation prescribed by the physician is used for protracted periods without his knowledge. Argyria from the use of these preparations has been reported; Berkley reports two more cases. The unsightliness and irremediable character of the ailment are sufficient to urge more care in the use of these preparations by physicians. Patients or parents should be warned of their dangers.

BONAR, Salt Lake City.

"AGRANULOCYTOSIS." JOSEPH E. SCHAEFER, J. Am. Dent. A. **21**:943 (June) 1934.

In this article, which deals with the etiology, symptomatology and treatment of agranulocytosis, the author states: "It would seem reasonable to consider that

there is both a primary and a secondary form of agranulocytosis; in other words, that there is a disease which attacks the bone marrow the nature of which we do not know and which we call primary, but that the bone marrow may be affected secondarily in an exactly similar manner by infections and toxins whose origin we do know."

Schaefer also mentions the frequency with which the condition follows extraction of teeth. In one of the cases cited the condition followed Vincent's infection which had been treated with neoarsphenamine.

NOYES, Chicago.

SOY BEAN AS A POSSIBLE IMPORTANT SOURCE OF ALLERGY. W. W. DUKE, J. Allergy **5**:300 (March) 1934.

Five workers in a soy-bean mill who suffered from cough and asthma were found to be sensitive to soy-bean extract. Sensitivity was passively transferable, and sensitized areas could be desensitized by other members of the legume group in one of the patients.

Increasing small doses of soy-bean extract gave definite relief in one case.

Soy-bean products are used for two hundred and fifty or more purposes, some of which are mentioned, which may make the soy-bean a cause of asthma in regions other than around the mill.

HOYER, Cincinnati.

RELAPSING FEVER IN CALIFORNIA: II. IMMUNITY. GEORGE E. COLEMAN, J. Infect. Dis. **54**:1 (Jan.-Feb.) 1934.

Coleman came to the conclusion that the strains that cause California relapsing fever are different from Spirochaeta Duttoni and possibly from Spirochaeta Novyi. Mice can be immunized by the three strains isolated by him, although their serums are not highly neutralizable in vitro. Passive protection was relative and absolute in only two instances.

TOOMEY, Cleveland.

CHRONIC SIALODOCHITIS. HENRY S. MEYER, J. Pediat. **4**:248 (Feb.) 1934.

A case of chronic inflammation of the ducts of the salivary glands is described. The patient was a 6 year old boy of Italian-Irish descent. His mother and maternal grandmother had apparently had the same condition. The use of epinephrine and large doses of alkalis always caused the salivary glands to decrease in size. Positive cutaneous reactions to spinach, bacon and paprika were found. When these foods and chocolate were removed from the diet there were no attacks. For eight months there was no swelling or pain in the salivary glands unless these foods were eaten. On the removal of these foods, relief was immediate.

LEMASTER, Evanston, Ill.

THE EFFECT OF EXTRACT OF PREGNANCY URINE UPON HYPOPITUITARISM IN THE MALE. RALPH H. KUNSTADTER and LOUIS S. ROBINS, J. Pediat. **4**:774 (June) 1934.

Eight boys, from 5 to 15 years of age, with a condition diagnosed as hypopituitarism were given hypodermic injections of 100 rat units of a purified form of the anterior pituitary-like sex hormone from the urine of pregnant women three times weekly for from three to six months. The purpose of the study was to determine the effect of anterior pituitary sex hormone from the urine of pregnant women on the genital development, obesity, growth of stature and metabolism. Descent of the testes occurred in all three cases of cryptorchism. In three cases characterized by genital underdevelopment, treatment resulted in enlargement of the testes and scrotum and the appearance of the secondary sexual characteristics. In four of five cases the basal metabolic rate was lower at the end of the treatment than before. The blood cholesterol changes were variable. In seven of the eight cases there was an increase in growth of stature above the normal. There was no loss of weight, nor was the distribution of fat typical of hypopituitarism altered.

LEMASTER, Evanston, Ill.

ACUTE HEMOLYTIC ANEMIA IN CHILDHOOD. ALEXANDER S. MANNE and LAWRENCE KUSKIN, J. Pediat. **4**:789 (June) 1934.

The case of an 8 year old boy with acute severe hemolytic anemia of the Lederer type is reported. The condition was characterized by a sudden onset with high fever, jaundice, leukocytosis, marked anemia and hemoglobinuria. Prompt recovery followed one blood transfusion. The presence of apical systolic and aortic diastolic hemic murmurs was considered interesting.

LEMASTER, Evanston, Ill.

STATUS THYMICOLYMPHATICUS. MARTIN SZABADOS, J. Pediat. **4**:798 (June) 1934.

The author cites experimental data and clinical facts in support of the theory that asphyxia is the cause of status thymicolymphaticus. The hypothesis is advanced that the rôle of the thyroid in status thymicolymphaticus is compensatory in regard to a primary asphyxial cause. All the different causative factors which are known to stimulate the thyroid merge into one principle—that of primary asphyxia—which is antecedent to the rise of the basal metabolic rate. The mechanism of sudden death in status thymicolymphaticus is discussed.

LEMASTER, Evanston, Ill.

THE MAINTENANCE REQUIREMENTS OF MYXEDEMA PATIENTS; CLINICAL AND CHEMICAL ASSAY OF COMMERCIAL THYROID PREPARATIONS. J. LERMAN and W. T. SALTER, J. Pharmacol. & Exper. Therap. **50**:298 (March) 1934.

Several preparations of thyroid extract from different sources were tested on twenty patients with myxedema. There was considerable variation in the activity of these preparations. Lerman and Salter conclude that the method of standardization of thyroid extract recommended by the United States Pharmacopeia, i. e., on the basis of the total iodine content, is the most satisfactory. (The abstractor has found that a satisfactory method is to give the patient's caretaker six months' or a year's supply of the sample of the extract tested on him. This insures uniformity of dosage and avoids frequent standardization.)

PILCHER, Cleveland.

DIABETES IN CHILDREN AND IN ADULTS PAST THE AGE OF FIFTY YEARS. HENRY J. JOHN, M. Clin. North America **17**:987 (Jan.) 1934.

The answers to a series of pertinent questions concerning diabetes in childhood and in later life are deduced from observation of a group of patients over a period of several years and briefly reported in this paper. In the young, the onset of diabetes was found to follow constantly in the wake of an acute infection. The rate of progress of the disease in the aged is much less rapid and is more easily controlled by proper treatment than in young subjects. John observed that the insulin requirements of all his adult patients except one diminished. The young patient, on the other hand, requires relatively more insulin, and his requirements tend to increase.

In children the chief enemy is infection, which may produce coma within twenty-four hours, even in a mildly diabetic child who requires no insulin. In children in whom extreme fluctuations in blood sugar occur, which cannot be controlled or stabilized by any amount of insulin, John believes the condition to be due to a deficiency of storage of glycogen in the liver. Fatty changes in this organ are found at necropsy in such cases.

In spite of the peculiar dangers which beset young diabetic patients John is optimistic as to their future.

EUGENE SMITH, Ogden, Utah.

NEUROFIBROMATOSIS IN CHILDREN: REPORT OF TWO CASES. COLIN C. STEWART, New England J. Med. **210**:150 (Jan. 18) 1934.

The first patient described, aged 16 years, has typical cutaneous neurofibromatosis or molluscum fibrosum, with the *café au lait* spots usually associated with

this condition. Her coarse features, large mouth, large hands and feet and her height, which is greater than that of her three sisters, suggest mild acromegaly. The mental signs are not pronounced enough to warrant a definite diagnosis, but fit in with the other features of Recklinghausen's disease.

The coexistence of ichthyosis and neurofibromatosis in the second patient, aged 12 years, emphasizes again the probability of a defect in the germ plasm controlling neurocutaneous development.

GENGENBACH, Denver.

HEREDITY AS A FACTOR IN THE ETIOLOGY OF DIABETES MELLITUS. P. J. CAMMIDGE, Lancet **1**:393 (Feb. 24) 1934.

Of 1,000 patients with diabetes, 396 showed an ancestral or family history of this disease. In 197 of these the disease was probably recessive, or familial, and in 199 it was probably dominant, or direct.

At present one can only state that heredity is a factor in the etiology which has to be reckoned with much more seriously than has been previously supposed. Since the potentiality for diabetes may be transmitted either as a mendelian recessive character or as a mendelian dominant character, it is necessary that the investigation of the history of diabetic patients should include that of the history of all blood relatives. Differentiation of the recessive from the dominant type is of some clinical importance, since the dominant variety is almost invariably mild and is easily controlled by diet alone, whereas the recessive form is generally grave from the onset and almost invariably requires the use of insulin to keep it under control.

LANGMANN, New York.

SEXUAL PRECOCITY IN A GIRL AGED THREE YEARS. ALICE KING, Proc. Roy. Soc. Med. **27**:414 (Feb.) 1934.

The mother of the patient stated that the child grew pubic hair at the age of 1 year, and that in the following two years the breasts developed and she grew rapidly in height. Menstruation began a few days before admission to the hospital and lasted only one day. She was extremely self-conscious and had no idea how to play with other children, but her intelligence was about normal. Her physical condition was good. Palpation of the abdomen under anesthesia revealed nothing abnormal.

WILLIAMSON, New Orleans.

ATROPHY OF THE TESTIS FOLLOWING NEONATAL ORCHITIS (? INTRA-UTERINE TORSION). HELEN MACKAY, Proc. Roy. Soc. Med. **27**:417 (Feb.) 1934.

The patient was a Jewish boy, aged 17 months. Delivery and pregnancy had been normal. The mother's Wassermann reaction was negative. The condition at birth and the subsequent history up to admission to the hospital are reported. On examination the patient was found to be well nourished, and the various systems failed to reveal any abnormalities. He had been circumcised. The left side of the scrotum was empty, and invagination of the left inguinal canal gave the impression that it was empty also. The right testis was in the scrotum and was normal.

WILLIAMSON, New Orleans.

OBESITY FOLLOWING SYDENHAM'S CHOREA. LEWIS THATCHER, Tr. Med.-Chir. Soc. Edinburgh, p. 27, 1933; in Edinburgh M. J., February 1934.

Thatcher mentions the fact that abnormal obesity is a recognized sequel to certain disturbances of the nervous system, particularly lethargic encephalitis. He showed a girl of 8½ years who was of normal size before chorea, but who had gained 26 pounds (11.7 Kg.) nine months after recovery. A loss of 12 pounds (5.4 Kg.) occurred just before a second attack, but she again acquired obesity after this relapse.

Thatcher remarks that obesity occurs seldom after rheumatic chorea; it was present in only seven patients in Coburn's series of 3,000 rheumatic subjects. Chorea would be logically expected in this disease in which the neuropathy is similar to that in encephalitis.

NEFF, Kansas City, Mo.

SUBACUTE MYELOID LEUKEMIA. LEWIS THATCHER, Tr. Med.-Chir. Soc. Edinburgh, p. 28, 1933; in Edinburgh M. J., February 1934.

An 11 year old girl had an unusual condition for a child—chronic leukemia, with no leukocytosis early and with the blood showing definite changes in both the red and white cells, which was well designated as erythroleukemia.

During the course of the disease from beginning anemia, with half the normal number of red cells, 30 per cent hemoglobin and about 10,000 white cells and with much irregularity in the size and shape of the cells, the spleen developed to a great size, nearly filling the abdomen. After this an increasing number of nucleated red cells appeared, the majority of which were megaloblasts. The number of leukocytes rose to 22,000. The proportion of immature granular cells reached 45 per cent; many of these showed mitosis. The late changes in the blood formula are ominous, Thatcher concludes, and suggest an increased disorganization of the reticulo-endothelial system.

NEFF, Kansas City, Mo.

INFLUENCE OF INTERCURRENT INFECTIONS ON THE COURSE OF KALA-AZAR. PAUL GIRAUD and ROBERT POINSO, Arch. de méd. d. enf. **37**:81 (Feb.) 1934.

Visceral leishmaniasis has become endemic at Marseilles, and sufficient material is continually available to permit one to note the influence of various agents on the evolution of this formidable disorder. The effect particularly of acute infectious processes superimposed on this chronic disease has provided some interesting data. In certain cases disastrous consequences promptly ensue; in others there is a distinct amelioration of symptoms, with lower temperatures or actual apyrexia and noticeable diminution in the size of the spleen. Ten cases are discussed in the authors' elaborate review.

AMESSE, Denver.

CLINICAL DIAGNOSIS OF TRACHEOBRONCHIAL ADENOPATHIES. KADRI RACHID, Arch. de méd. d. enf. **37**:213 (April) 1934.

Of the two methods employed in the diagnosis of mediastinal and tracheobronchial adenopathies—roentgenologic and stethoscopic—Rachid believes that the latter is undeniably superior in the early stages and before organic changes have advanced to a point where they are readily discernible on the x-ray film.

Glandular hypertrophies in the cavity of the chest constitute newly forming tumors in a state of phlegmasia. Auscultation brings out not only the signs bearing the names of Heubner, Smith and Marfan, but a new one described here by Rachid for the first time. He calls it the sign of respiratory silence produced by compression of a large bronchus the area of distribution of which no longer gives the normal vesicular murmur. This condition was verified at autopsy in several instances, and specimens are on exhibit at the pathologic museum of the University of Istanbul.

Another sign detected by auscultation is a pleural friction rub with a fine souffle arising in the pulmonary tissues, which is best heard in the right or left subclavicular spaces, the first and second intercostal spaces and the interscapular space close to the median line, in the latter site especially after a light cough. Rachid asserts that these phenomena are produced by vasodilation and passive hypervascularization of the tissues contiguous to the area of phlegmasia and recommends that the diagnosis be verified by the cutireaction of Pirquet.

AMESSE, Denver.

ACUTE LEUKEMIA WITH ULCERONECROTIC ANGINA: REPORT OF A CASE. CONSTANTIN KIZOULIS, Arch. de méd. d. enf. **37**:217 (April) 1934.

A case of acute leukemia with predominating pharyngeal phenomena is reported in a Greek boy of 9 years. The initial symptoms—an intense chill followed by moderate fever—appeared twenty days before admission to the hospital; two days later the child complained of severe pain in the pharynx, which was not particularly exaggerated on deglutition, and a short time later the parents noted tumefaction of the submaxillary lymph nodes. The breath was foul. A temperature of from 102 to 104 F. characterized the subsequent course of the disease; there were marked pallor and great prostration, with complete loss of appetite.

About the nineteenth day definite necrosis of the oral and pharyngeal tissues began, and on the following day a purpuric eruption appeared over the face and body. Examination revealed moderate hypertrophy of the liver and spleen; the blood picture showed 3,200,000 red cells, anisopoikilocytosis with polychromatophilia, and 9,600 white cells, 52 per cent of which were polymorphonuclear neutrophils, 3 per cent eosinophils, 28 per cent lymphocytes, 13 per cent large mononuclears, 2 per cent metamyelocytes and 2 per cent myeloblasts. Intensive treatment with arsenicals, calcium chloride, local douches and antidiphtheritic serum failed to stay the progress of the disease or to alter in the least degree its malignant character; extravasations of blood continued, and the patient died on the thirtieth day. Permission for an autopsy was not obtained.

AMESSE, Denver.

CHRONIC ABDOMINAL PAIN FROM LAMBLIA INTESTINALIS. A. GUERSTEIN and J. REYDERMANN, Arch. de méd. d. enf. **37**:463 (Aug.) 1934.

A rather unusual source of abdominal pain has been revealed through the use of the duodenal tube in clinical practice. Nothnagel, in 1892, first discussed the rôle of the flagellate Lamblia intestinalis in the development of disorders of the alimentary tract; most authors since that time (Dobell, Sdrodovsky, Bach and Kiefer) have declared that the presence of these parasites in the human intestine is so nearly universal that their influence must be almost purely a mechanical irritation of the mucous membrane.

In 1919, however, Lyon was able to identify these flagellates in the bile ducts, and later Westphal and Georgi, among others, reported a number of cases of invasion of the liver, with varied clinical manifestations; the syndrome of cholecystitis or cholangeitis was common. Certain infestations seem to involve the nervous system particularly.

Guerstein and Reydermann report five cases in which the bile, recovered through the duodenal tube, showed great numbers of Giardia.

AMESSE, Denver.

HEMORRHAGIC DIATHESIS IN THE COURSE OF PURPURA HAEMORRHAGICA. A. LANDAU and W. HEJMAN, Presse méd. **42**:174 (Jan. 31) 1934.

Landau and Hejman, after a detailed study of a case of purpura haemorrhagica (Werlhof), conclude that there is no connection between the appearance of purpura and hemorrhages from mucous surfaces and the platelet count and bleeding time. In their case of grave thrombopenia complicated by cerebral hemorrhages there were periods during which, in spite of a total absence of platelets and bleeding time of 60 minutes, there was no cutaneous purpura or mucosal hemorrhage. They believe that the contractility of the blood vessels compensates for the penury of the platelets and accounts for the transition from the thrombopenic diathesis into the latent state.

BIEKER, St. Petersburg, Fla.

TRACHEOBRONCHIAL ADENOPATHY AND HOCHSINGER'S SIGN IN CHILDREN AFTER THE SECOND YEAR OF LIFE. C. DEMURTAS, Riv. di clin. pediat. **32**:129 (Feb.) 1934.

Hochsinger's sign is positive if one or more lymph glands are palpable over the thoracic wall, extending down from the axilla by the pectoral muscle to the fifth

interspace. In children under 2 years of age such glands are not palpable unless there is some intrathoracic chronic infection, usually tuberculous tracheobronchial adenitis. Hochsinger found palpable thoracic glands in 52 of the 1,542 children under 2 years of age whom he examined; in 37 the glands were palpable on both sides, and in 15 on only one side.

DeMurtas, in examining 600 children of from 2 to 12 years of age, found a positive Hochsinger's sign in 35; the glands were palpable on both sides in 8 and on one side in 27. Only 11 (32 per cent) had a positive tuberculin reaction. Hochsinger's sign is of little importance for the diagnosis of tuberculous tracheobronchial glands, DeMurtas concludes, except to suggest other more accurate studies. He gives a carefully worked out outline for the systematic diagnosis of tracheo-bronchial tuberculous adenitis.

HIGGINS, Boston.

LIPOID NEPHROSIS IN CHILDREN. E. INGLESSI, Riv. di clin. pediat. **32**:178 (Feb.) 1934.

This article is a review of the literature and the present conceptions regarding lipoid nephrosis in children.

HIGGINS, Boston.

COMPLICATIONS OF INFANTILE KALA-AZAR. J. M. SALA GINABREDA, An. de pediat. Barcelona **1**:26 (Jan.) 1934.

Among chronic complications of kala-azar are amebiasis, syphilis and tuberculosis. Among the infectious complications gangrenous stomatitis, bronchopneumonia, endocarditis, and nephritis and pyelitis are frequent. The blood is almost always attacked by the parasite by way of the hematopoietic organs, and profound anemia results. Lastly, certain complications may result in the diagnosis and treatment. Occasionally a child has convulsions following splenic puncture, although this procedure is necessary for diagnosis in most instances and is good practice. Intolerance to antimony is not uncommon, and the initial symptoms of nausea, vomiting and a rise in temperature should lead to its discontinuance.

SANFORD, Chicago.

SYMPTOMS OF CHRONIC HYPERTENSIVE NEPHRITIS IN THE CHILD. P. NOBÉCOURT, Arch. am. de med. **10**:2 (Jan.) 1934.

This condition is rare in childhood. Permanent arterial hypertension is the most characteristic and constant symptom. The onset is insidious. The earliest symptoms are subjective and functional, such as headaches, abdominal pains and disturbances of vision. The headache and abdominal pain are often accompanied by vomiting. Eclamptic or convulsive seizures may occur. Vision may be either blurred or entirely lost. Other symptoms which may occur are epistaxis, palpitation, dyspnea and attacks simulating asthma. Polyuria and nocturnal enuresis are commonly present. The urine contains no blood or leukocytes and only occasionally a hyaline cast and a moderate amount of albumin.

The excretion of phenolsulphonphthalein is reduced to 30 per cent or even as low as 5 per cent. Edema is rarely observed. There is a constant increase in the urea content of the blood. Chlorides may or may not be retained. The constant hypertension eventually results in increased cardiac volume. There is also dilatation of the arch of the aorta. The child always shows pallor and wasting, and there is some dwarfing. The duration of the disease is from one to five years. The outcome is always fatal.

The cause of the disease is unknown, although syphilis seems to be a factor in some cases. Renal dysplasia is advanced as a possible cause by the author.

SCHLUTZ, Chicago.

LIPOID NEPHROSIS. C. INCLAN, Arch. de med. inf. **2**:154 (April) 1933.

Lipoid nephrosis is not rare. In order to establish a diagnosis it is necessary to determine the clinical syndromes. The most valuable symptoms are inversion

of values for the blood proteins, decrease of the osmotic pressure of the proteids, cholesteremia and positive results of renal function tests. The lack of red cells in the urine, together with a high degree of albuminuria, leads to the diagnosis. Measurement of the basal metabolism is of no value, on account of the edema. In most of the cases the etiology is unknown. The prognosis is not as favorable as some investigators lead one to believe. Lipoid nephrosis should be considered a grave condition. The treatment is doubtful, dietetic measures are the most important.

SANFORD, Chicago.

SYNDROME OF THE DISPLACED HEART. PEREZ DE LOS REYES, Arch. de med. inf. **3**:525 (March) 1934.

In the syndrome of the displaced heart one finds displacement of the centers of auscultation, characteristic roentgen changes, changes in the electrical axis, atypical waves in electrocardiograms and variations in height of the R peaks, which show considerable shrinking or decrease during inspiration or expiration. In cases of sudden displacement there are collapse, cold sweats, cyanosis and fall in the arterial pressure.

The etiology may be supradiaphragmatic or infradiaphragmatic. In the former the causes are intrabronchial or extrabronchial. Intrabronchial causes are curds, vomitus, mucus, blood or foreign bodies in the airways, which in turn cause atelectasis of one or several lobes of the lung. Shifting of the trachea toward the large atelectatic shadow is a sign of this. Among the extrabronchial causes are atelectasis itself or tumors that compress a bronchus, effusions or pneumothorax. The infradiaphragmatic causes are tumors, cysts, ascites or any increase in gaseous pressure within the stomach or splenic angle of the colon. Traumatism and falls may also cause this.

The prognosis depends on the electrical axis of the heart; a deviation toward normal shows improvement. Treatment should consist of inhalations of oxygen and carbon dioxide. This precludes the production of atelectasis.

SANFORD, Chicago.

MONILETHRIX IN A CHILD OF SIX YEARS. JOSÉ DE CASTRO PALOMINO, Arch. de med. inf. **3**:578 (March) 1934.

The symptoms of this condition and the literature are reviewed. The case presented was in a boy of 6 years. There was no familial history of the disease. This is the first case described in the Cuban medical literature.

SANFORD, Chicago.

INDICANEMIA AND THE UREMIC SYNDROME. PERFECTO A. SAINZ, Arch. de med. inf. **3**:604 (March) 1934.

Sainz reports a case of acute postscarlatinal nephritis with a uremic syndrome in a boy of 11 years. The condition did not have the usual course, for a decrease in blood urea did not follow clinical improvement. There were no particular clinical improvement and no diminution in the value of the blood indican. The method of Grigaut was employed to estimate the blood indican. These values are of great importance in the prognosis in acute as well as chronic cases. There is a bibliographic review of indicanemia.

SANFORD, Chicago.

CERVICAL ADENOPATHY IN INFANCY. ROBERTO VALDÉS DÍAZ, Arch. de med. inf. **2**:265 (April-June) 1933.

The author gives a good differential diagnosis of cervical adenopathy. He reports a case of Hodgkin's disease in which the following interesting blood picture was found: eosinophils, 11 per cent; basophils, 0; myelocytes, 2 per cent; juvenile

forms, 0.5 per cent; stab cells, 22 per cent; segmented cells, 54 per cent; large lymphocytes, 4.5 per cent; small lymphocytes, 6 per cent, and large mononuclears, 0. Red cells numbered 3,770,000, with 78 per cent hemoglobin with a color index of 1.03.

HERRON, Spokane, Wash.

UNUSUAL FINDINGS IN CELIAC DISEASE. ANGEL HEBRERO, Pediatría españ. **22**:771 (Dec.) 1933.

Hebrero reports unusual degrees of anemia in two cases of celiac disease. The hemoglobin was 22 per cent in one case and 28 per cent in the other. The blood state and picture resembled the clinical picture seen in the chlorosis of puberty. There were marked alterations in the water metabolism, with a tendency to edema. Hebrero relates some of the clinical findings to endocrine dysfunction in these cases and believes that the sexual glands are in some way involved.

SCHLUTZ, Chicago.

ETIOLOGY OF URINARY INFECTIONS IN CHILDREN. RAYMUNDO MONIZ DE ARAGAO, Pediatria, Rio de Janeiro **1**:81 (April) 1934.

This article contains a review of the literature and a report of the results of cases seen by the author. The points emphasized are the occurrence of urinary infections almost exclusively in girls, the digestive symptoms or associated gastrointestinal disorders and the fact that other organisms than Bacillus coli may be found to be the cause of such infections.

SANFORD, Chicago.

INTRATHORACIC CYSTIC LYMPHANGIOMA. O. MICHAELS, Deutsche Ztschr. f. Chir. **242**:250 (Jan. 8) 1934.

Lymphangioma is the most uncommon of thoracic tumors. Most mediastinal lymphangiomas are related to cystic hygromas of the neck, which may indicate that they represent downgrowths. True intrathoracic lymphangiomas are, however, because of both their position and origin, to be grouped separately from cystic hygromas of the neck, which are perhaps related in origin to faulty closure of the branchial clefts. Michaels briefly reviews three cases already reported in the literature. The age of the first patient is not stated. The other patients were women, 48 and 60 years of age, respectively. The author's case was that of an 8 month old child who had had some respiratory difficulty from birth, which was most marked, however, since the age of 6 weeks. This child had marked stridor, rapid respirations, swelling of the veins of the neck and retractions of the thorax. On crying there was marked bulging of the soft tissues of the suprasternal and supraclavicular fossae. There was marked dulness in the upper mediastinal region, extending into both pulmonary fields. No râles could be heard in the upper or lower pulmonary fields. The middle areas presented numerous râles. The roentgen rays showed a large, round mass in the upper mediastinal region, which was thought to be a thymic tumor. Because of the great respiratory distress, an operation was performed immediately under ether anesthesia. A large cystic tumor was found which could not be completely removed but which was considerably reduced in size by incision and drainage. The respiratory difficulty was relieved, but the child died the second day after the operation. At necropsy no other congenital anomalies were observed. The tumor mass was shown to consist of three main cystic structures with numerous smaller cysts. Photographs of the gross structure are shown, and the microscopic anatomy is described. Michaels states that whereas most thoracic cysts can be completely dissected out, this is usually impossible with lymphangiomas. They are usually accompanied by numerous smaller cysts which it is impossible to find and remove completely, and these may cause a recurrence of the condition.

GLASER, Rochester, N. Y.

A Pernicious-Like Anemia in Childhood. Otto Iseli, Folia haemat. **51**:223, 1933.

The author reports anemia of eight months' duration in a child 9 years of age. The child had recurrent attacks of vomiting, became weak and tired easily. Examination of the blood eight days before death showed: red cells, 850,000, with 15 per cent hemoglobin, and white cells, 2,800, with polymorphonuclear neutrophils, 24.33 per cent; basophils, 0.33 per cent; monocytes, 1.33 per cent; lymphocytes, 70 per cent; plasma cells, 1.33 per cent; normoblasts, 0.33 per cent, and myelocytes and metamyelocytes, 1 per cent. There were marked anisocytosis, poikilocytosis and polychromasia. Gastric analysis showed hydrochloric acid of 40 and a total acid of 60. Necropsy showed hemosidern in the spleen, liver and bone marrow and marked fatty changes in the myocardium, liver, kidneys and subdural and pericardial hemorrhages. The bone marrow was red and very nuclear; few erythrocytes were found, but fair numbers of nucleated red cells, normoblasts and megaloblasts were present. The greater number of cells were neutrophilic myelocytes. Eosinophils, as well as groups of lymphoid cells, were also found. There was considerable hemosiderin in the spleen.

McBryde, Durham, N. C.

Rare Ocular Changes in Schüller-Christian Disease: Report of a Case. P. A. Jaensch, Klin. Monatsbl. f. Augenh. **92**:158 (Feb.) 1934.

Jaensch describes some rare ocular changes in a boy, aged 10, with all the symptoms of Schüller-Christian disease: defects in the skull, exophthalmos and diabetes insipidus. Numerous small xanthomas in the epidermis, especially of the lids, were found; furthermore, there were lipoid granulomas of the conjunctiva and the limbus corneae and a similar formation on the disk. Partial fatty degeneration, similar to interstitial keratitis, seen in the cornea, was diagnosed as a primary deposit of lipoid. The formation at the limbus, with a diameter of 6 mm., did not involve the cornea; it was interpreted as a granuloma with a secondary deposit of lipoid, analogous to that in Ceelen's case.

Considerable changes took place in the course of six months: The fatty degeneration of the cornea, receded, while the individual spots in the cornea grew larger, assuming a silvery-white hue. Small dark-brown spots developed in the macula, which had been free from hemorrhages and other changes hitherto; the formation in the disk remained unaltered but for slight periodical variations of its thickness. The Wassermann and Pirquet reactions were negative.

Stoll, Cincinnati. [Arch. Ophth.]

Influence of Salyrgan on the Galactose Test. H. Bix and L. Wechsler, Med. Klin. **29**:1642 (Dec. 1) 1933.

Previously, Bix and Wechsler demonstrated that the glycosuria of both diabetes mellitus and diabetes phlorhizin is reduced by the administration of salyrgan Now they show that the galactosuria following the ingestion of 40 Gm. of galactose is greatly reduced by the administration of salyrgan. This is true for both normal persons and for those with damage to the liver.

Dooley, New York.

Chronic Intestinal Disturbance with Decalcification of Bones in an Adult and Its Relationship to Celiac Disease of Childhood. H. Wendt, Med. Klin. **30**:187 (Feb. 9) 1934.

Wendt presents a complete report of a case of a disease similar to celiac disease of children in a 39 year old woman. There were marked enteritic changes, especially in the small intestine. Roentgenograms showed fluid level shadows, when taken without a contrast medium, but when taken with barium sulphate showed normal emptying of the stomach and irregular filling of the intestine, with both retarded and accelerated passage. Bacterium coli was recovered from the duodenum. Despite normal pancreatic and biliary secretions, there were definite

disturbance of protein and carbohydrate metabolism and marked disturbance in resorption of fat. The patient had osteoporosis with spontaneous fractures, hypocalcemia, hypophosphatemia, tetanic manifestations and a tendency to acidosis. The blood sugar curve was low following a dextrose tolerance test. Hypochromic anemia and leukopenia were part of the picture.

DOOLEY, New York.

CASE OF KALA-AZAR FOUND IN A NATIVE CHILD BORN IN NIU-CHUANG, MANCHOUKUO. T. BUTO and Y. YAMAMOTO, J. Orient. Med. **21**:12 (July) 1934.

A case of kala-azar in a native child of Niu-Chuang, Manchukuo, aged 6 years, was verified, and splenectomy was done. The spleen was carefully examined histologically, and the following conclusions were reached:

1. Kala-azar seems to be widespread in Manchukuo.

2. The decrease of erythrocytes and leukocytes in the case studied was obvious; the decrease in leukocytes was particularly noteworthy.

3. The number of monocytes increased, while the neutrophil leukocytes were greatly reduced. The hemoglobin content was also reduced.

4. Among the histologic changes, hypertrophy of the reticular cells was obvious. Dilatation of the sinusoids and hypertrophy and hyperplasia of the sinusoidal endothelial cells were also marked. Numerous endothelial cells were desquamated in the lumen of the sinusoid, but there were few erythrocytes in it.

5. Leishman-Donovan bodies were particularly numerous in the reticular cells and were also visible in the endothelial cells of the sinusoids.

EDITOR'S SUMMARY.

CLINICAL PROPHYLAXIS OF ERGOTISM. S. GAISSINOWITCH, E. KOENIGSBERG and A. KOGAN, Vrach. delo **17**:438, 1934.

On the basis of their own observations, as well as of data in the literature, the authors distinguish three forms of ergotism brought about by the use of bread containing cecale cornutum: the convulsive form, the gangrenous form and the mixed form. In the first form there is sometimes a so-called pregangrenous stage, which is characterized by regression of morbid phenomena.

The most frequent form is the convulsive, which manifests itself in a characteristic clinical picture. The symptoms of intoxication appear between the first and twentieth day after the use of bread containing ergot and consist in vertigo, general weakness, somnolence, paresthesias and gastro-enteritic troubles. Then, after from two to three days, cramps appear in the flexor musculature of the hands and feet, which are very painful. In two patients there were psychic symptoms, such as excitement, restlessness, increased motor activity and sometimes epileptic fits. The gastro-enteritic disturbances consist in vomiting, profuse diarrhea and abdominal pains. They were observed in one half of the cases studied and, as the observations at autopsy showed, were related to pathologic changes.

The authors discuss further the therapy and prophylactic measures which are to be taken in order to prevent the development of ergotism.

YAMPOLSKY, Atlanta, Ga.

A NEW THERMOTHERAPEUTIC METHOD—PARAFFIN THERAPY. A. R. KIRICHINSKI, E. G. KICHINA and J. I. MINTZ, Vrach. delo **17**:487, 1934.

The therapeutic value of paraffin is based on the physical qualities of this substance (compressibility, elasticity, conductibility of heat), which make it fit for hot applications in certain diseases, mostly those of rheumatic origin. The founder of the paraffin treatment method was Barthe de Sandfort, who used it as early as 1910 in Paris. But in the United Soviet State of Russia this method is not sufficiently known or used as yet. The authors have used it since 1932 in a

somewhat modified form; instead of pouring paraffin on the affected extremity, they put the member into melted paraffin in a specially fitted box. This modification has the advantage of transmitting more heat to the tissues. Even small changes in the pulse rate and body temperature are observed; perspiration is more abundant, as the sittings are repeated, and this is accompanied by marked relief of pain. Every sitting lasts about from one-half to one hour. The authors studied two hundred cases in which the patients were treated according to this method and found a marked improvement of the condition in about eighty, or 40 per cent. In eleven, or 6 per cent, no changes were noted, and in three there was a change for the worse.

YAMPOLSKY, Atlanta, Ga.

CLINICAL CONTRIBUTIONS CONCERNING THE USE OF BLOOD TRANSFUSION IN PEDIATRICS. I. L. RAIGORODSKI and E. M. TURCHINA, Vrach. delo **17**:390, 1934.

The authors used blood transfusion in two cases: (1) a case of aleukemia haemorrhagica and (2) a case of anemia pseudoleukaemica, with but temporary success in both, and do not recommend this treatment in grave conditions. Blood transfusion is indicated in chronic disturbances of nutrition when the presence of any decompensating process can be excluded by a careful analysis of the case and in cases of grave subchronic troubles of nutrition presenting some manifestations of toxicosis but without signs of strong intoxication. Blood transfusion is particularly indicated in infectious diseases of long duration which are apt to produce grave troubles of nutrition.

YAMPOLSKY, Atlanta, Ga.

CHANCES OF DETECTING INFECTIONS WITH INTESTINAL PROTOZOA. R. SVENSSON and F. J. LINDERS, Acta med. Scandinav. **81**:267 (March 6) 1934.

Among a group of persons known to be heavily infected with intestinal protozoa, seventy-four were subjected to an exhaustive examination for the presence of infections. Fifty-nine were found to be harboring one or more protozoal species.

Suspensions of stools were examined, unstained, stained with Heidenhain's iron-hematoxylin method and Quensel's methylene blue-cadmium-sudan method. The last mentioned method has been found absolutely reliable for the diagnosis of trophic amebas.

Statistical analysis of the collected data proved that even six examinations of formed stools from each person in a series did not reveal constant proportions of the actually existing infections. Ten examinations per case were sufficient.

KAJDI, Baltimore.

USE OF THE DUODENAL SOUND FOR THE INTRODUCTION OF FLUID. L. O. FINKELSTEIN, Acta pædiat. **15**:252 (March 28) 1934.

Finkelstein believes that the problem of administering adequate fluid to sick infants has not been solved satisfactorily by most of the methods now in vogue and presents a lengthy plea for the use of the duodenal sound. His own technic specifies a Nélaton no. 12 or 14 catheter graduated into 10 cm. divisions and fitted with a record syringe by means of which fluid may be either instilled or aspirated. The catheter is introduced by the oral route for a distance of from 20 to 25 cm.; gastric peristalsis is relied on to carry the tip into the duodenum. Fluoroscopic control in several cases showed that this is achieved when the catheter has descended 25 or 30 cm. The time required for the tip to enter the duodenum is usually from twenty-five to thirty minutes, but may be as short as from five to ten minutes. The location of the tip can be verified by noting the type of fluid aspirated or by auscultating the abdomen while fluid is being introduced. If the tip has reached the duodenum injected fluid cannot be aspirated, whereas it can be recovered promptly from the stomach.

The superiority of this method is said to consist in the fact that larger quantities of fluid can be introduced without producing vomiting. It is a more

natural method than those that employ parenteral routes. It does not exclude the liver from early participation in the metabolism of the administered fluid. This is a point the importance of which has been recognized only recently. Furthermore, many clinicians believe that fluid given by mouth is more effective in combating conditions of dehydration than that given by other routes. It is of considerable advantage that the apparatus for this procedure need not be sterilized.

McCune, New York.

Schönlein-Henoch Disease. G. Schetelig, Finska läk.-sällsk. handl. **76**:264 (March) 1934.

In the first of Schetelig's patients, a girl, aged 4½ years, the disorder set in with pronounced abdominal pain, diarrhea and vomiting and was followed by repeated eruptions of purpura, subcutaneous edema, pain in muscles and in the extremities and, finally, hemorrhagic nephritis. There were violent reactions against proteins and animal albumin, following both parenteral and oral administration. The second patient, a boy of 16 years, presented a far milder form of the disease, with typical outbreaks of purpuric patches. In the third patient, a man, aged 24, the disease was characterized by long continued hemorrhagic nephritis. Treatment with a diet deficient in albumin and with preparations of papaverine-anolan-atropine derivatives gave good results.

Elghammer, Chicago.

Collapse of the Lung and Atelectatic Bronchiectasis in Childhood. M. de Bruin, Nederl. tijdschr. v. geneesk. **77**:5345 (Dec. 2) 1933.

At roentgen examination a triangular shadow is sometimes seen, situated in the medio-inferior part of the lung. Hitherto it has been taken to indicate pleuritis mediastinalis inferior. Reports from the literature and the author's own observations would prove that this shadow is often brought about by collapse of the lower lobe of the lung or a part of this lobe. Attention is drawn to the combination of collapse of the lower lobe and bronchiectasis in the atelectatic region of the lung. This combination is described in the literature as atelectatic bronchiectasis. Probably collapse occurs first, bronchiectasis developing afterward in the atelectatic lobe.

van Creveld, Amsterdam, The Netherlands.

Nervous Diseases

The Autonomic Nervous System. Eric A. Linell, Am. J. Psychiat. **13**:926 (March) 1934.

A summarized account of the structure and functions of the autonomic nervous system is presented, including a discussion of some of the recent experimental work on the proof of the presence of centers in the hypothalamic area of the diencephalon. Linell believes it probable that many current views will have to be modified in the future. This small area of the brain is at present much studied.

Jahr, Omaha.

The Cerebral Circulation. Stanley Cobb, Am. J. Psychiat. **13**:947 (March) 1934.

It is generally believed that the cerebral arteries are end-arteries and do not anastomose, and that there is no vasomotor control of cerebral vessels. Experimental evidence exists that justifies a revision of this belief. It is true that the cerebral vasomotor mechanism is less active than the vasomotor mechanism in other organs, but there is ample proof that vasoconstriction and vasodilatation occur. That the ganglion cells are very sensitive to oxygen needs is surmised from the great richness of the capillary supply. When the carotid and vertebral arteries in a cat are clamped for from eight to twelve minutes convulsions set in. The

convulsion is the result of profound cellular changes in the cortex, especially in the layers of greatest vascularity. In man, it is estimated that complete anemia of eighteen seconds will cause a convulsion. A case is reported of a patient suffering from typical jacksonian epilepsy. At autopsy the cortex of the left motor area showed pallor, with necrosis of the nerve cells. It is argued "that partial anemia is more likely to cause fits than complete anemia, also that a small focal area of such anemia is more likely to produce status epilepticus than a large area."

JAHR, Omaha.

THE BLOOD SUGAR IN RELATION TO EMOTIONAL REACTIONS. J. C. WHITEHORN, Am. J. Psychiat. **13**:987 (March) 1934.

This report describes a twelve year study of emotional reactions in the patients of a small hospital for persons with mental disorders. Nine hundred and forty-five nondiabetic patients were included, and during fasting the blood sugar levels were compared with the blood sugar determinations during or following a stage of excitement. There is a discussion of the present knowledge of carbohydrate metabolism in the psychoses, with the conclusion that emotional excitement produces rarely, if at all, any rise in the blood sugar level during fasting. Melancholic reactions appear to depress somewhat the insulinogenic function of the pancreas. Ordinarily this depression of function is demonstrable only as a moderately delayed demobilization of dextrose, under a load, so that the blood sugar during fasting falls within normal limits, except in a few persons, usually older than 45, whose capacity is already somewhat limited by diabetes or some other organic disease.

JAHR, Omaha.

NOTE ON A "PROTEOSE-LIKE" SUBSTANCE IN SPINAL FLUID. PURCELL G. SCHUBE and RICHARD C. WHITEHEAD, Am. J. Psychiat. **13**:1083 (March) 1934.

The spinal fluid from thirty-seven unselected patients, both normal and with pathologic conditions, was studied. In all the cases ether-alcohol extracts yielded a proteose-like substance not hitherto recognized in the spinal fluid. The nature of this body is being further investigated.

JAHR, Omaha.

CLINICAL STUDIES OF MENTAL TESTS. SIMON H. TULCHIN, Am. J. Psychiat. **13**: 1237 (May) 1934.

The acceptance of the findings in mental tests at their face value by the clinical psychologist may lead to serious consequences. The results of the tests depend on too many variables in the surroundings of the child to be in themselves alone reliable. This is particularly true of the Stanford-Binet test. The factors which influence the proper interpretation of the reported intelligence quotient are divided into four groups:

1. Performance in the test. This is influenced by the physical condition of the child, his language experiences, race and nativity, social and economic surroundings, previous medical history, special abilities and disabilities.

2. Limitations inherent in the tests. The special advantages and disadvantages of training have an influence. Early training in the recognition of colors, counting coins, giving the name and other training may vitiate the results of the test, unless interpreted in the light of the social and intellectual background of the child tested.

3. Comparison of the results of several different types of examinations, performance tests and educational achievement tests.

4. Criteria of intelligence based on other standards than the results in the tests with particular reference to the school history, developmental history, the opinions of teachers and others and the psychiatric examination.

These four factors to be considered in interpreting the intelligence quotient in tests and retests are reported, with pertinent findings, and the importance of evaluating data obtained from other members of the clinical team is emphasized.

JAHR, Omaha.

HISTOPATHOLOGY OF THE CENTRAL NERVOUS SYSTEM IN EPIDEMIC ENCEPHALITIS. ARTHUR WEIL, Arch. Neurol. & Psychiat. **31**:1139 (June) 1934.

Histologic study of the brains of patients who died of encephalitis during the St. Louis epidemic indicated:

(1) There were acute disseminated encephalitis and myelitis, accompanied by mild leptomeningitis.

(2) The histologic picture was the same as that in other epidemics of epidemic (lethargic) encephalitis. There were perivascular infiltration by small round cells and a few plasma cells and isolated areas of proliferated glia. The nuclear masses of the thalamencephalon and midbrain were more affected than either the cortex or the areas of the brain stem.

(3) The fact that clinically meningitis manifested itself first and that histologically this was most pronounced at the base of the brain and especially in the interpeduncular fossa suggests a possible spread of the infection along the pial sheaths into the brain.

(4) None of the cranial nerves showed evidence of inflammation.

(5) In three cases of eight studied, colonies of small cocci (measuring from 0.3 to 0.6 micron) were observed in the proliferating glia within thrombosed blood vessels or intermingled with the perivascular cellular exudate.

BEVERLY, Chicago.

ENCEPHALOMALACIA IN INFANTS. I. B. DIAMOND, Arch. Neurol. & Psychiat. **31**:1153 (June) 1934.

Diamond reports two cases of cerebral softening in infants. The first child had attacks of athetoid movements with hyperextension and spasticity of all the extremities. The date of onset was unknown, but ocular changes were noted several weeks after birth. The eyes showed arrested development, microphthalmia, prenatal iridocyclitis and retinal detachment. In the brain were extensive foci of softening, cavities, atrophy of the right hemisphere and reactive aseptic meningitis. The cavities indicated an advanced softening, which evidently was present at birth. A history of trauma at birth was not obtained. The second case was that of a 3½ month old child who had convulsions following diarrhea. After apparent clinical recovery the patient was taken home, but was brought back a month later in convulsions and died. Autopsy showed marked edema of the leptomeninges and hyperemia and edema of the brain. After fixation in formaldehyde the section showed numerous foci of softening in the cortex of all the lobes.

Diamond concludes that while cerebral softening in infants is considered most commonly to be due to trauma at birth, the condition in the first case was in all probability due to infection and that in the second to intoxication.

BEVERLY, Chicago.

CEREBRAL BLOOD FLOW PRECEDING AND ACCOMPANYING EPILEPTIC SEIZURES IN MAN. F. A. GIBBS, W. G. LENNOX and E. L. GIBBS, Arch. Neurol. & Psychiat. **32**:257 (Aug.) 1934.

It has been generally considered that epileptic seizures are caused by cerebral anemia resulting from cerebral vascular spasm. The authors attempted to investigate this hypothesis by measuring the blood flow of the jugular vein by inserting a thermo-electric blood flow recorder. In none of the ten patients studied was there a significant reduction in the blood flow immediately preceding the onset of the seizures. During severe convulsions there was a great increase in the flow, which was considered a result rather than a cause of the seizure. The evidence is therefore against the theory that there is widespread anemia of the brain which causes convulsions.

BEVERLY, Chicago.

A Note on the Occurrence and Significance of Air in the Subdural Space After Encephalography. Fritz Cramer, Bull. Neurol. Inst., New York **3**:506 (March) 1934.

Cramer reports a case proving that air may pass into the subdural space after intralumbar injections of air. In the case reported a trephine opening showed a large amount of air underneath the dura and outside the arachnoid following encephalography.

Beverly, Chicago.

Meningococcus Meningitis: A Further Clinical Study. Maxwell P. Borovsky, Illinois M. J. **64**:532 (Dec.) 1933.

Three hundred and thirty-eight consecutive cases of meningococcic meningitis are reported with reference to mortality according to the patient's age and color, the day of the illness on admission to the hospital, the clinical picture, the type of treatment, the prognostic significance of certain symptoms and complications, the laboratory findings and the reports of reexaminations made months after the patient's discharge from the hospital.

The fact that among these 338 cases there were only 11 instances of more than 1 case in a family sustains the epidemiological fact that meningococcic meningitis is only mildly contagious. Borovsky believes that the high mortality (57.1 per cent) among this group is due to the fact that many of the patients entered the hospital in such a serious condition that they had little opportunity to show any response to therapy. The mortality was highest in patients under 2 and over 40 years of age. The lowest mortality occurred in those aged from 4 to 5 and from 6 to 8 years. In 32 patients petechiae were present. Borovsky points out that the death rate in this group is the same as the general mortality, in contradistinction to the prevalent idea that these cases offer a much more serious prognosis than cases without a hemorrhagic tendency. Seventy per cent of the patients with chills as a part of the clinical picture died. Of unusual interest and what seems paradoxical to every one who is at first confronted with this information is the fact that the more severe the opisthotonos the better the prognosis. Borovsky believes that the degree of opisthotonos is in a measure proportionate to the basilar involvement.

Negative Brudzinski and Kernig signs were observed in 11 and 12 cases, respectively, and usually in the more severe cases, as evidenced by the mortality of 75 per cent. The average cell count on admission was 10,456. The lowest count was 600, and the highest 74,000. The differential cell count in every instance was recorded as indicating polymorphonucleosis. The results of globulin tests were universally positive. The blood showed leukocytosis in every case. Antimeningococcic serum of the polyvalent variety was used in the treatment of these patients. No difference was found in the therapeutic value of any of the brands employed. To make certain of obtaining adequate drainage cisternal puncture was immediately resorted to when lumbar puncture was becoming inadequate. The average amount of serum used in cases in which the patient recovered was 188 cc., given intrathecally. Routine daily intrathecal injections of serum were continued until the fluid became clear, with a diminution in the cell count to a few hundred. Daily spinal drainage was continued until the pressure returned to normal and the cell count fell to 100 or less.

Antimeningococcic serum was administered intravenously to 40 patients. The mortality in this group was 65 per cent. Borovsky thinks that the efficacy of this form of therapy must be questioned. His figures show an increase rather than a decrease of mortality in the patients who received antimeningococcic serum intravenously in addition to intraspinal injections. Deafness was the outstanding sequela.

Barbour, Peoria, Ill.

A Few Remarks on Brain Functions. G. Vercellini, J. Nerv. & Ment. Dis. **79**:301 (March) 1934.

This article is a review of the definitely known functions of the thalamus, the corpus striatum and the cortex, as shown by studies in anatomy, physiology and

pathology, as well as a discussion of possible developments in this field. Conscious perception of certain sensory elements, cenesthesia, intellectual functions, memory and other functions are interpreted in terms of functions of the thalamus and associated with cortical and striatal activities.

JAHR, Omaha.

SCAPULAR TENDON REFLEXES. SAMUEL WEINGROW, J. Nerv. & Ment. Dis. **79**:391 (April) 1934.

A review of the history and principles of the tendon reflex, together with a discussion of reflex action in general, is submitted. The scapular region lends itself particularly to reflex testing, since it is out of sight of the patient; and no reinforcement is necessary, as is often the case in the patellar region, where the patient predicts the tap. Also, the depressions between the scapula, the ribs and the spinal column offer a good arrangement for elicitation of stretch reflexes. The tendons tapped are the rhomboideus, minor and major, the supraspinatus, the infraspinatus and the teres major. Anatomic diagrams and photographs illustrate the technic.

JAHR, Omaha.

THE p_H AND LACTIC ACID CONTENT OF THE CEREBROSPINAL FLUID. I. HARRIS, C. W. JONES and C. N. ALDRED, J. Neurol. & Psychopath. **15**:46 (July) 1934.

Contrary to current teaching, the spinal fluid is not more alkaline than the blood. This belief, the authors state, is attributed to the faulty method of determining the p_H of the spinal fluid, with a disregard of the factors of carbon dioxide and temperature. By the use of the glass electrode in a room heated to body temperature twelve determinations were made. In each instance the p_H of the cerebrospinal fluid was lower than that of the blood, the average for the latter being 7.42 and for the spinal fluid, 7.36. The lactic acid content of the cerebrospinal fluid and the blood are approximately the same.

JAHR, Omaha.

BACILLUS ENTERITIDIS MENINGITIS IN AN INFANT OF FIFTEEN MONTHS. JOHN O. VAUGHN, J. Pediat. **4**:631 (May) 1934.

Bacillus enteritidis of Gärtner was identified as the causative organism in a fatal case of meningitis in a 15 month old infant. The history of diarrhea preceding meningeal symptoms, the finding of colitis at autopsy and demonstration of the organism in blood cultures point to the intestinal tract as the portal of entry and to the blood stream as the route by which the organisms reached the meninges.

LEMASTER, Evanston, Ill.

CONVULSIONS IN CHILDREN. HARRIS HOSEN, J. Pediat. **4**:636 (May) 1934.

The causes of convulsions in children are divided into five groups: toxic, organic, idiopathic, reflex and metabolic. Among forty-five cases of convulsions in children at the Touro Infirmary, in eighteen the causative condition was diagnosed as autointoxication, in three as epilepsy, in five as tetany, in one as cerebral injury, in one as acute tonsillitis and in one as syphilis. In sixteen cases no etiologic diagnosis was made. Immediate treatment to stop the convulsive seizures is strongly advocated.

LEMASTER, Evanston, Ill.

OPERATIVE TREATMENT OF INFANTILE HYDROCEPHALUS. R. G. DOUGHTY, J. South Carolina M. A. **30**:51 (March) 1934.

The object of this article is to show that some hydrocephalic babies, if operated on early, can be cured, thus relieving a burden on the state institutions.

"Hydrocephalus is caused by a structural defect which may be the result of malformation, trauma or infection." There is a discussion of the anatomy and physiology, with emphasis of the difference between the communicating (external) and the noncommunicating (internal) types. After the type is determined according

to the method described in the article, if the condition is favorable operation is done. Doughty cites one case of hydrocephalus in which operation was performed, with favorable results.

WESTON JR., Columbia, S. C.

THE TREATMENT OF ACUTE POLIOMYELITIS WITH THE RESPIRATOR. NEIL LOUIS CRONE, New England J. Med. **210**:621 (March 22) 1934.

This report is based on twenty-four cases of patients treated in the Drinker respirator at the Massachusetts General Hospital, from 1931 to 1933. They are divided into three groups, depending on the primary cause of respiratory failure: (1) those with involvement of the respiratory muscles, (2) those with involvement of the bulbar "centres" and (3) those with involvement of both mechanisms. There were nine patients with involvement of the respiratory muscles. Of these, five died. Two of the four survivors have been followed for two years and are invalids confined to bed. The other two have been followed for one year; one of these is completely paralyzed in the legs, arms, and trunk and is confined to bed; the other shows sufficient recovery to justify the hope that she may walk with the aid of braces and crutches.

There were ten patients with bulbar involvement. In all these the outcome was fatal. There were five patients in the third group. Of these, three died; one is in braces, after two years, with almost no use of the arms, and the other has extensive paralysis of the arms, legs and trunk and spends all night and two hours during the day in the machine.

GENGENBACH, Denver.

NEW DEVELOPMENTS IN THE CARE AND TRAINING OF MENTAL DEFECTIVES. CHARLES L. VAUX, Psychiatric Quart. **7**:673 (Oct.) 1933.

Among the newer and more gratifying developments in the care of the feeble-minded Vaux lists: (1) extension of an educational program so that every child may have educational opportunities equal to his capacity, avoidance of a chronologic maximum age or minimum mental age as a criterion of admission to the institutional school and placement according to scores of achievement tests; (2) training classes in domestic arts designed to instruct the patients in service in a small home (to be distinguished from training in an institutional kitchen or bedroom service); (3) occupational therapy on a par with academic work, seasonal, individualized and thoughtfully planned; (4) classes in habit training to make up for the defective habit training supplied by inadequate parents or poor environment; (5) physical training to develop health, grace, coordination, balance and interest; (6) colony houses in the village outside the institution which the inmate may use as a half-way station, in which he may adjust himself gradually to community life and in which he may find a social center and a source of help and advice, and (7) boarding in private families. These developments give increasing hope of returning many defective persons as assets to a community in which they had formerly been nuisances, liabilities or menaces.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

HYPERINSULINISM AND EPILEPSY: PRESENTATION OF PATIENTS AND CASE REPORTS. SEALE HARRIS, South. M. J. **26**:1026 (Dec.) 1933.

The author reports cases in which hyperinsulinism has been seen to produce the syndrome of epilepsy. In some cases adenoma of the islands of Langerhans was present; in other cases the condition was due to overactivity of the pancreas. The patients were successfully treated by a diet relatively low in carbohydrate and high in fat. This treatment was particularly effective if the patient was underweight.

If convulsive seizures cannot be controlled by diet, Harris suggests the use of surgical intervention. The operation consists of either the removal of the adenoma of the islands of Langerhans or resection of a part of the pancreas. Operations on the pancreas, however, should not be undertaken until it is proved

that the convulsions are due to insulogenic hypoglycemia and cannot be controlled by dieting. The dietary regimen should be adjusted to the patient's nutritional state and can be well controlled only by a short stay in a hospital.

If hypopituitarism is a factor, the pituitary hormones can be given. In giving the pituitary hormones it is advisable to examine the urine for sugar and check up on the blood sugar every few days, because excessive doses can produce glycosuria and hyperglycemia.

SCHLUTZ, Chicago.

A STUDY OF CHILD'S SLEEP. GLENVILLE GIDDINGS, South. M. J. **27**:312 (April) 1934.

Giddings, from his experiments, reaches the following conclusions regarding normal sleep:

In a child accustomed to retiring early the soundest sleep comes before midnight. Any physical discomfort, whether it be pain or some other factor, markedly interferes with sound sleep. Fever, per se, interferes little with sleep.

Antipyretics which are given for the reduction of fever and which reduce the fever may be associated with an increase in movement during sleep. Whether this increase is due to the antipyretic or the decrease in the fever is unknown.

SCHLUTZ, Chicago.

CASE OF LATE INFANTILE AMAUROTIC IDIOCY. B. SCHLESINGER, J. A. GREENFIELD and R. O. STERN, Arch. Dis. Childhood **9**:49 (Feb.) 1934.

A case of amaurotic family idiocy in a child who died at the age of 22 months is reported. A detailed histologic description of the nervous system is given. The nerve cells presented the swollen ballooned appearance characteristic of this disease. This swelling was due to distention of the cells by deposition in them of a lipoid substance. Histochemical tests showed this to be a compound of cerebrosides and phosphatides, occupying an intermediate position chemically between normal myelin and neutral fat. Similar swellings were observed on many axons of nerve cells; in some situations, notably in the frontal and occipital cortex, these axonal swellings were larger than the cells. Intense gliosis was present in the superficial layers of the cerebral cortex and of the cerebellum and also in the optic thalamus and round the ventricles. There was degeneration of the frontopontine and the pyramidal fibers and of some fibers of the optic nerve. There was a loss of ganglion cells in the retina. Greenfield and Stern compare the disturbance of lipoid metabolism with that in Niemann-Pick disease.

KELLY, Milwaukee.

RELATION BETWEEN EPILEPSY AND CONGENITAL SYPHILIS. W. H. DE B. HUBERT, Brit. M. J. **1**:530 (March 24) 1934.

Mention is made of the supposed relationship between syphilis and epilepsy, and the pedigree of a family is followed for three generations. There were two epileptics, one in the second generation and one in the third. In one of these cases it is suggested that there is a possible relationship between syphilis and epilepsy.

ROYSTER, University, Va.

NEUROGENIC TUMORS OF THE SYMPATHETIC SYSTEM IN CHILDREN. J. W. S. BLACKLOCK, J. Path. & Bact. **39**:27, 1934.

Of a series of malignant tumors in children those arising from the sympathetic system were fourth in order of frequency. In the eighteen tumors with this origin different stages in the development of the cells were observed, from one composed of the most primitive type of sympathetic cells (sympathogonia) through an intermediate group in which many of the sympathogonia had differentiated into sympathoblasts and small ganglion cells to one composed only of mature ganglion cells. Indeed, in certain tumors transitional stages could be traced from small

embryonic cells to small and mature ganglion cells. In the remarkable (and indisputable) case described by Cushing and Wolbach (1927) this was observed to occur during the life of a child in whom a tumor of the dorsal region was diagnosed histologically as a sympathicoblastoma in the early years of life, while ten years later when the tumor was removed surgically it had become an adult ganglioneuroma. The intermediate group was the commonest type in the series, which is in agreement with most of the reported cases. I have suggested a simple scheme for the classification of these growths according to the degree of differentiation of their cells.

From the Author's Summary and Discussion. [Arch. Path.]

An Outbreak of Acute Anterior Poliomyelitis. C. D. Brink, South African M. J. **8**:560 (Aug. 11) 1934.

Of 17 patients admitted to the hospital during the epidemic at Bloemfontein eight (47 per cent) died. In all the fatal cases there was the ascending type of paralysis. Reports of all types of cases are given, and the clinical manifestations, therapy and prophylaxis are discussed. Brink believes that vaccination with the attenuated virus will be the method of prevention in the future.

Gonce, Madison, Wis.

Agoraphobia in a Child of Twenty Months Beginning with First Attempts at Walking. Kadri Rachid, Arch. de méd. d. enf. **37**:161 (March) 1934.

The case of a Jewish boy, 20 months of age, exhibiting the syndrome of agoraphobia, or the fear of the open places, is reported from the children's division of the medical school and hospital at Istanbul.

Physical examination gave entirely negative results; the child was strong and vigorous, with no history of accident, injury or illness, but the family history showed that the paternal grandmother was suffering from the same phobia. The patient could walk normally if supported lightly by the hand, but lost confidence at once when entirely alone and fell to the floor. The diagnosis was verified by Prof. Kérim of the psychopathologic division of the University of Istanbul.

Amesse, Denver.

A Case of Encephalitis Followed by Deafness. S. Gracoski, Bull. Soc. de pédiat. de Iasi **5**:3 (Jan.-March) 1934.

An infant, 14 months old, began to have convulsions after five days of fever, diarrhea and vomiting and lay in a stuporous state for several days. Lumbar puncture revealed apparently normal cerebrospinal fluid. Paresis of the right upper eyelid developed. The child's general condition improved greatly, but diminution in vision and hearing persisted.

LeMaster, Evanston, Ill.

Two Cases of Pneumococcic Meningitis in Infants. E. Hurmuzache, Bull. Soc. de pédiat. de Iasi **5**:11 (Jan.-March) 1934.

Two cases of pneumococcic meningitis in infants are reported, with observations at autopsy. One case is that of an infant 9 months old, the other that of an infant 3½ months old. In both instances meningitis set in during the course of bronchopneumonia.

LeMaster, Evanston, Ill.

Possible Association of Little's Disease and Muscular Dystrophy. L. Babonneix and C. Roederer, Bull. Soc. de pédiat. de Paris **31**:142 (March 21) 1933.

A girl, 3½ years old, showed marked involvement of the pyramidal tract, evidenced by stiffness of the lower extremities with spasm of the adductors, which is characteristic of Little's disease; exaggerated reflexes, and clonus and Babinski

plantar responses bilaterally. There were also suggestive signs of muscular dystrophy, such as waddling gait, lordosis, slight hypertrophy of the muscles of the calf, difficulty of the patient in raising herself to the standing position and a questionable alteration in the response to electrical stimulation of the left quadriceps. The child was to be observed further before a definite diagnosis of muscular dystrophy could be made.

BENJAMIN, Montreal, Canada.

EVOLUTION OF CELLS IN THE CEREBROSPINAL FLUID IN CASES OF MENINGOCOCCIC MENINGITIS TREATED WITH SERUM. B. TASSOVATZ, Rev. franç. de pédiat. **10:** 121, 1934.

Twenty-six cases of epidemic cerebrospinal meningitis have been studied and are presented chiefly from the point of view of changes in the cerebrospinal fluid. The changes are due to irritation by the infecting organism and its toxins, to the effect of the serum used in the treatment and to the effect of the serum on the infection. In general, following the treatment the number of cells and the percentage of polymorphonuclears decrease until one has a clear fluid, but continued use of the serum after the infection is overcome may lead to the persistence of large numbers of polymorphonuclears. In this event a negative culture is the indication for stopping treatment.

The cases may be divided into five groups: In the first the condition is relatively benign and is characterized by rapid and progressive diminution in the number of cells and the percentage of polymorphonuclears. From three to five injections of serum suffice for recovery. In the second group the condition is more severe and there is a less rapid decrease in the number of cells and the percentage of polymorphonuclears. The injection of serum during from six to eight consecutive days is necessary. The third group, that of severe infections treated during the first week and mild infections in which treatment was begun later, shows an increase in cells following the first and second injections, then a decrease and finally a stationary phase in which the cells number from 400 to 500, with 70 per cent polymorphonuclears. It is in such a stage that the interruption of serum therapy is useful. The last two groups include the noncurable forms. In the first of these the organisms persist in spite of treatment, and the cells remain at about 1,000, with from 80 to 90 per cent polymorphonuclears. Death occurs at the end of from two to three weeks. In the last group, that of severe cases in which treatment was begun late in the course of the disease, the condition seems to be made worse by the use of serum. The cells increase after each injection and diminish only as injections are stopped or death approaches. Because of this type of reaction it is suggested that the first dose of serum in such cases be relatively small and diluted in physiologic solution of sodium chloride. The usual dose given throughout this study was 20 cc. injected intraspinally or intramuscularly.

LESLIE, Evanston, Ill.

EVOLUTION OF THE NERVOUS SYSTEM IN THE INFANT AND YOUNG CHILD. CLAIRE VOGT, Rev. franç. de puériculture. **2:**14 (Feb.) 1934.

Until the age of 3 months the infant has only sensation and reflex actions. Between the ages of 3 and 6 months classification begins: localization of sounds distinction of persons and objects and affective manifestations. Between the ages of 6 and 30 months come dentition, walking, speech and sphincter control. The tendon reflexes become less exaggerated, but hypotonia and other evidences of pyramidal insufficiency are present until about 30 months. After 30 months these infantile neuromuscular characteristics should have disappeared, and the child should have acquired a certain degree of affectivity and activity and the ability to use the personal pronoun correctly.

CRANE, Chicago.

REFLEXES OF THE NEW-BORN AND NURSLINGS. P. VALENTINI, Clin. pediat. **15:**959 (Dec.) 1933.

After a general discussion of the neurologic-anatomic findings in young infants, the author reviews the various reflexes which may be demonstrated in this age

period and calls particular attention to the fact that babies in the first stage of life are to be regarded as being in a "sub-cortical" state, so far as the nervous system is concerned. Studies of the "extra-pyramidal" phenomena of Poussep, Schrywer-Bernhard, Boveri and Piotrowski are described for a group of normal children ranging in age from 2 months to 11 years. There is an excellent bibliography.

DOOLEY, Kent, Conn.

HEMATO-ENCEPHALIC BARRIER IN INFANCY. BRUNO PINCHERLE and GIUSEPPE SALOM, Pediatria **42**:239 (March 1) 1934.

This paper discusses fully the present status of knowledge concerning the hemato-encephalic barrier. Permeability of the barrier to acid fuchsin was studied in fifty-six infants under 13 months of age and was found to be present in 100 per cent of those under 3 months of age. It decreases during the following 6 months, and by the end of the first year the barrier behaves as in the adult. Pincherle and Salom suggest that this increased physiologic permeability of the barrier is probably due to immaturity of the tissues at birth. They express the opinion that this permeability is not responsible for the tendency of infants to have convulsions or meningitis, but believe that it may be one of the causes which bring about the changes found in the cerebrospinal fluid in congenital syphilis, as well as cerebral complications in intestinal intoxication.

SIGNORELLI, New Orleans.

TREATMENT OF CHOREA WITH PHENYL-ETHYL-HYDANTOIN. LEON VELASCO BLANCO and HECTOR ABRINES, Arch. am. de med. **10**:8 (Jan.) 1934.

The authors report cases of chorea in four patients ranging in age from 8 to 11 years, who were treated with phenyl-ethyl-hydantoin. The best result was obtained in the case in which treatment was begun early. In the other cases the duration of the attack was shortened. Whether the drug was given in one dose or in fractional doses did not seem to make any difference in the effect.

The rash caused by phenyl-ethyl hydantoin begins on the extremities and then extends to the trunk and head, differing from the rash of measles in respect to the usual site of appearance and distribution. The eruption is usually transitory. No untoward symptoms were observed in any of the cases.

SCHLUTZ, Chicago.

MYOCLONIC ENCEPHALITIS. MAMERTO ACUNA and AGUSTIN N. ACCINELI, Arch. argent. de pediat. **4**:641 (Sept.) 1933.

The authors report a case of this condition in a child 10 years old and express the belief that it is a myoclonic form of lethargic encephalitis. Incoordinate movements occurring during both waking and sleeping were prominent symptoms. There was no defect in speech. The neurologic lesions in this condition are in the anterior horns of the medulla. No form of treatment seemed to give any relief of the symptoms.

SCHLUTZ, Chicago.

TWO CASES OF PROGRESSIVE MUSCULAR DYSTROPHY. A. G. DA SILVA, Arch. de pediat., Rio de Janeiro **6**:553 (Feb.) 1934.

Two cases of this condition, accompanied by illustrations, are described.

SANFORD, Chicago.

RESIDUAL DIAPHRAGMATIC HEMIPLEGIA IN THE CHILD. J. DE CARDENAS, Pediatría españ. **22**:794 (Dec.) 1933.

A case of this rare condition is reported in a tuberculous child aged 11 years. Paralysis of the left side of the diaphragm was complete and presented the clinical picture seen in a phrenectomized patient. The physical signs were puzzling and

suggested the presence of fluid in the left side of the chest. Extensive tuberculous hilar changes on both the right and the left part of the mediastinum were doubtless responsible for the development of the condition. SCHLUTZ, Chicago.

TOXIC ENCEPHALITIS FOLLOWING USE OF THALLIUM ACETATE. F. POZZO and M. J. TARQUINA, Prensa méd. argent. **21**:374 (Feb. 21) 1934.

A child 7 years old had typical toxic encephalitis. Thallium acetate in normal doses had been used. The spinal fluid was normal, as was the blood. In addition to the symptoms of encephalitis the child lost all her hair, as is usual in thallium poisoning. Pozzo and Tarquina discuss the toxicology of thallium compounds, review the literature and warn against their use. SANFORD, Chicago.

SIGNIFICANCE AND SEQUELAE OF CONVULSIONS DURING INFANCY AND CHILDHOOD. EMIL VON LEDERER, Arch. f. Kinderh. **102**:1 (April 27) 1934.

Three hundred and twenty infants and children who had one or more convulsions were studied over a four year period. In 56.2 per cent of these the convulsion first appeared during the first year of life, in 18.2 per cent when they were from 1 to 3 years old, in 9.4 per cent when they were from 3 to 6 years old and in 16.2 per cent when they were from 6 to 15 years old. More than one convulsion occurred in 77.2 per cent of the children. Of those who had only one convulsion 65 per cent were less than 1 year old. No bad results were seen following one convulsion unless the illness causing the convulsion was very severe. The most severe consequences occurred in the children who had the most convulsions and in those in whom the convulsions began at a very early age. Frequently epilepsy was first manifested at the onset of an acute febrile attack. The most common sequelae of convulsions were mental deterioration, psychic changes, hydrocephalus, microcephalus and cerebrospastic diplegia. LEMASTER, Evanston, Ill.

TREATMENT OF CEREBROSPINAL MENINGITIS. F. W. STRATMANN, Med. Klin. **29**:1513 (Nov. 3) 1933.

Stratmann reports a case of meningococcic meningitis in which the disease progressed unchecked while specific intrathecal injections of antitoxin were being given but seemed to yield readily to three intravenous injections of a nonspecific protein. DOOLEY, New York.

DISTURBANCE OF SPEECH AND HEREDITY. GUTZMANN, Med. Klin. **30**:256 (Feb. 23) 1934.

Of 325 stuttering patients examined in less than two years (Berlin), approximately one-third had a family history of disturbance of speech. Gutzmann suggests that a predisposition toward this defect of speech may be a negative characteristic. During the same period 353 patients who stammered were examined in the same clinic. Only about 5 per cent of these had a family history of disturbance of speech. Several genealogical tables showing an apparent relationship between the functional disturbances of speech in these patients and a familial tendency to neuropathic states are presented. DOOLEY, New York.

LATE RESULTS OF THE LEIPZIG EPIDEMIC OF POLIOMYELITIS OF 1927. ERICH HASSLER, Monatschr. f. Kinderh. **59**:256, 1934.

Hassler examined one hundred and fifteen patients with poliomyelitis five years after the epidemic and compared the findings with those obtained six months after the illness. A great majority of patients showed no change. In a few there was definite improvement in some muscles which had been considered totally paralyzed. Disturbances in growth and size were common and did not seem to parallel the severity of the paralysis. In a few children there was deterioration of muscle

function, and paralyses occurred in muscles which had not originally appeared diseased. In no child was there a recurrence. Mental and meningeal symptoms were absent.

GERSTLEY, Chicago.

A CASE OF MENINGITIS CAUSED BY BACILLUS ENTERITIDIS (GÄRTNER). PETER SCHMITT, Monatschr. f. Kinderh. **59**:269, 1934.

Schmitt reports the case of a 3 month old baby who was dying of acute meningitis. The disease lasted two weeks. The organism isolated from the spinal fluid was identified as Bacillus enteritidis (Gärtner) by cultural and serologic methods, as well as by animal experiment.

GERSTLEY, Chicago.

MEDICAL TREATMENT OF EPILEPSY. EMIL VON LEDERER, Monatschr. f. Kinderh. **59**:359, 1934.

Lederer follows the reasoning of Karger, namely, that the indicated treatment is that with a drug causing dilatation of the cerebral vessels. If the symptoms are produced by vasospasm, drugs like caffeine might give good results. Accordingly he tried several proprietary remedies which are claimed to be vaso-antispasmodics. Such treatment benefited sixteen patients.

The reviewer cannot overlook the fact that these children also received phenobarbital in doses of from 2 to 3 grains (0.13 to 0.19 Gm.) daily, plus bromides.

GERSTLEY, Chicago.

TETANY ON A FRESH FOOD DIET. O. BAUMER, Monatschr. f. Kinderh. **60**:336, 1934.

The title of this article is misleading. Babies were fed a synthetic mixture devised by Bircher as a substitute for breast milk. Apparently the food is an emulsion of powdered almonds with various fruit juices. Tetany developed in infants on the diet, which the author ascribes to its low calcium content.

GERSTLEY, Chicago.

BLOOD GROUPING IN POLIOMYELITIS. K. HATSKY, München. med. Wchnschr. **80**:1973 (Dec. 15) 1933.

The blood groups to which patients with poliomyelitis belong were determined by Grooten and Kassovich in France and by Shaw, Thelander and Kilgariff in the United States. Among 78 French patients and the 100 from San Francisco none belonged to group AB. This group is found in only from 3 to 5.6 per cent of the population. Hatsky determined the blood groups of 131 patients with poliomyelitis and found that 1.5 per cent belonged to group AB. In comparison with the blood group of 9,111 patients with other diseases the results were:

Group	AB	A	B	O
Poliomyelitis	1.5	43.5	16.8	38.2
Control patients.....	3.2	46.6	6.8	43.4

BRAHDY, Mount Vernon, N. Y.

DIAGNOSIS AND THERAPY OF POLIOMYELITIS. J. SIEGL, Wien. klin. Wchnschr. **47**:237 (Feb. 23) 1934.

Siegl states that serum therapy is at present the only treatment of poliomyelitis from which real results can be expected. Since it seems to be effective only in the early stage, i. e., before the appearance of paralysis, an early diagnosis must be made. Poliomyelitis begins with a prodromal stage which gives the impression of an unspecific infection, and the diagnostic difficulties are increased by the variety of the symptoms in the initial stage. The first prodromal symptoms appear after a period of incubation of from seven to ten days and are usually

expressed in a slight increase of temperature, nausea, headache and pharyngitis. There is usually constipation; diarrhea is rare. These symptoms last about one or two days, but the diagnosis cannot be made from them. After several days in which no symptoms are evident, the same disturbances set in and introduce the preparalytic stage. The symptoms are still not characteristic and seem to point to disturbances of the upper respiratory tract or of the digestive tract rather than of the central nervous system. The fever and the blood findings do not permit of certain diagnosis either, but this double onset of symptoms may, in times of an epidemic, awaken suspicion of poliomyelitis. Symptoms of spinal meningitis soon appear. One first finds rigidity of the neck and spinal column, general and local hyperesthesias and atactic tremors. The symptoms of meningitis usually are not so intense as in cases of tuberculous meningitis or even cerebrospinal meningitis. However, there are cases of poliomyelitis in which the condition also begins with violent meningeal symptoms. The pain is localized chiefly in the back, though sensitiveness to touch and pain on movement may be found in other places, especially in the lower extremities, where the paralysis later sets in. Certain nerve trunks may also be sensitive to pressure. In the further course of the preparalytic stage atactic tremors appear, usually in the legs. Conditions of weakness in the arms and legs may also be a sign of the approaching paralysis, likewise excessive outbreaks of sweating and evanescent red areas in the skin, which may have the form of exanthems. The preparalytic stage lasts from two to five days. There may be extremely few symptoms or none, so that the paralysis appears in a child apparently in perfect health. In all cases of suspected poliomyelitis lumbar puncture should be made, since the spinal fluid early shows inflammatory changes. The pressure is increased; the fluid is rarely clouded because of increase of cells, which is never great and consists chiefly of an increase in lymphocytes. The reactions for albumin are usually positive; the sugar content is normal or increased, but never decreased, which may be important for the differential diagnosis from other forms of meningitis. The reactions for colloid are not characteristic. Lumbar puncture never does any harm and can have only a good effect if the condition is really poliomyelitis.

In regard to therapy, convalescent serum is doubtless most effective. If possible, mixed serums should be used, since they have a more even value. The best route of administration is the intralumbar route (possibly following lumbar puncture), using from 10 to 20 cc. of serum. In addition, from 20 to 50 cc. of serum should be injected intramuscularly. If there is no convalescent serum at hand, animal serum can be used. Petit's horse serum is supposed to have had the best results. Its dosage is about the same as that of convalescent serum. The injection of serum can be repeated the next day, but there is no use in continuing it after the paralysis has set in. In serum therapy it is naturally supposed that serum will always be immediately available. In unexpected situations native adult blood, according to Busson and Hamburger, which is best taken from the parents of the child, can be injected, since it is assumed that most adults have antitoxins in their blood. The proper serum may be injected later. Schottmüller recommends blood transfusion, convalescents from poliomyelitis being chiefly considered as donors. The specific serum therapy can be supported by the administration of methenamine and by roentgen therapy and diathermy.

ABT, Chicago.

MOVEMENTS OF THE BABY DURING THE FIRST MONTH OF LIFE. V. W. D. SCHENK, Nederl. tijdschr. v. geneesk. **77**:2309 (May 20) 1933.

In studying movements of children it is insufficient to determine only the presence or absence of certain reflexes. The movements of small infants must be studied from the quantitative, as well as the qualitative, point of view, and in their relation to the functions of the growing organism. Schenk arrived at the following conclusions:

1. In examining the movements of the baby it is advisable to use the methods of Bersot (*Schweiz. Arch. f. Neurol. u. Psychiat.* **7**:212, 1920; **8**:24, 1921).

2. During the first month of life one finds adversive movements of the wrist and hand.

3. Catching with tonic after-contraction, without tonic after-contraction and movements of the wrist and hand in the direction of the stimulus form a coherent group of adversive mechanisms found during the first month of life in about 71 per cent of the infants observed.

4. There is a relation between catching and the nutritive functions.

VAN CREVELD, Amsterdam, The Netherlands.

Miscellaneous

PEDIATRIC PROGRESS DURING THE LAST FIFTY YEARS. LOUIS FISCHER, Arch. Pediat. **51**:207 (April) 1934.

A brief and interesting review of the progress in the pediatric field in the past fifty years is given. The advances in bacteriology, immunizations and allergic knowledge are recalled. The problem of infant feeding is briefly discussed with reference to lactic acid milk, percentage feeding, various fads and proprietary foods. Various procedures commonly used today, such as lumbar puncture, transfusion, anesthesia and the use of the roentgen rays, are presented historically. The discovery of the deficiency diseases, the use of gland extracts, the inspection of milk and the Credé method for the prevention of ophthalmia neonatorum all constitute chapters in the story of the advancement of pediatrics.

WADDELL JR., University, Va.

THE RURAL HEALTH MOVEMENT. C. C. APPLEWHITE, J. South Carolina M. A. **30**:123 (June) 1934.

A brief review of the public health work in the South is given in this article. The main problem is the improvement of rural sanitation. It is from the country districts that we derive our food, milk and water; consequently it is of the utmost importance that the base of supplies be kept clean. This can be done by the elimination of the contamination of the water supply, properly located and constructed privies and screening. This can be accomplished by the education of the masses in such a way that the people have a proper association with the well organized and well trained county health unit.

WESTON JR., Columbia, S. C.

THUMB SUCKING. IRENE G. WOODCOCK, M. Rec. **139**:328 (April 4) 1934.

Sucking may be present as an isolated habit or it may be concomitant with such habits as nail-biting, masturbation, enuresis and pica. In the article it is discussed in its isolated or simplest form. In the same category as thumb-sucking one must place lip-sucking, finger-sucking, the sucking of clothing and the sucking of a pacifier. The physiology, etiology and pathologic conditions caused by the habit and the consequences and treatment are all discussed by the author. In concluding, he states that he feels sure all thumb-suckers are not seekers of sexual excitement. Nevertheless, because of the physical danger involved in allowing the habit to develop, the tendency to glide over it as a meaningless performance must be decried. Most abnormal youthful tendencies can be corrected in time by imitation and social disapproval.

WILLIAMSON, New Orleans.

THE EARLY INFANTILE SEXUALITY OF MAN AS COMPARED WITH THE SEXUAL MATURITY OF OTHER MAMMALS. MAX LEVY-SUHL, Internat. J. Psycho-Analysis **15**:59 (Jan.) 1934.

There is evidence that infantile sexuality is a biologic remnant in the course of evolution of man. In one form or another man existed long before the glacial

period, and there is reason to suppose that sexual maturity came not in youth but in early childhood between the ages of 4 and 5. To support this theory Levy-Suhl refers to the evidence in the animal kingdom. There he finds that most cattle mature sexually before the age of 12 months. The only animal that matures at an age corresponding to that of maturity in human beings is the elephant; the male matures at the age of 20 years and the female at the age of 16. Histologic evidence shows that the female germ is substantially mature when the child is 5 or 6 years of age, but at this age a pause in development takes place because the rest of the soma of the girl is not ready for conception and reproduction. There is thus a period of latency between early childhood and youth which one also observes psychologically in psychoanalysis. The same biologic forces which operate in man in delaying mature sexuality also operate in the elephant. The elephant is rather unique in the animal kingdom and has practically no relationship to other species. The author believes that the data on mammalian phylogeny support the material which one observes in psychoanalysis.

KASANIN, Howard, R. I. [ARCH. NEUROL. & PSYCHIAT.]

STRYCHNINE POISONING IN A CHILD. C. PERRY, M. J. Australia **1**:812 (June 23) 1934.

A case of strychnine poisoning in a 3 month old baby was reported; the condition was found to be due to strychnine in the milk of cows grazing in a paddock where rabbits poisoned with strychnine had been burned. Chemical analysis of the cows' milk showed the presence of strychnine. The child improved when put on uncontaminated milk.

TENNEY, Madison, Wis.

HEREDITY AND DISEASE: THE STORY OF ABBÉ GILLET'S RABBITS. J. H. SEQUEIRA, South African M. J. **8**:369 (May 26) 1934.

In 1919 Abbé Gillet reared in a pure state a new breed of rabbit, dystrophic as to the growth of fur, nails, ears, feet, head and vibrissae, which he named Castorrex. It was soon shown that the castorrex features are a recessive mendelian character and obey Mendel's law of heredity. Then it was held that the mutations in utero which produce the peculiar characteristics of Castorrex are the result of infection with Treponema cuniculi. If this is true it is the first recorded instance in which dystrophies produced by an infection have followed the laws of heredity and opens a new field of speculation. It suggests that certain heredodystrophies due to human syphilis may also follow Mendel's laws; that hereditary syphilis may result from the direct effect of the treponema (in a virus stage) on a gamete, chromosome or even a gene; that syphilis of the third generation is possible, and that "cellular" syphilis, which present methods of investigation are unable to recognize but which produces functional disturbance, may actually occur.

GONCE, Madison, Wis.

DENTAL CARIES. A. WILCKEN, Progrès méd., July 28, 1934, p. 1220.

This article is chiefly a review of Bunting's work on the relationship of the bacillus acidophilus to dental caries. It is suggested that further information may be obtained from a study of the chemistry of the saliva as well as from the alimentary regimen.

LESLIE, Evanston, Ill.

A CURIOUS FORM OF COCAINE POISONING. F. J. COLLET, Rev. d'oto-neuro-opht. **12**:281 (April) 1934.

A girl, aged 7 years, manifestly degenerated (difficulties of speech, strabismus and facial asymmetry), following the packing of the nose with 10 per cent solution of cocaine exhibited atypical signs of poisoning. There was no pallor or weakness of the heart, though the pulse rate was 150. The child did not speak and

did not struggle with the nurse but exhibited automatic movements of suction, mastication and dancing or marching round and round. Collet suggests that the effect of the cocaine was to bring about relative inhibition of the cortex, which accounts for the mutism and the predominance of the action of the optostriate body, which presides over the elementary movements for self-preservation: suction and mastication. DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

HEIGHT AND WEIGHT OF ADOLESCENT BOYS AND GIRLS IN THE YEARS 1929-1932. SIGISMUND PELLER, Wien. klin. Wchnschr. **47**:683 (June 1) 1934.

Peller reports the average measurements of about 30,000 persons aged from 14 to 16 and compares them with the "normal" measurements of Kornfeld. The sexual differences of growth are discussed.

Adolescent boys are thinner than adolescent girls and have a smaller index of bodily fulness (the index was calculated according to Rohrer) and less weight per centimeter of height. Boys show greater departures from the average measurements in height and in weight than girls, though the departures in weight are less marked.

In the years 1929 to 1932 the adolescent boys and girls were found to be better developed than in the first years after the World War and in the pre-war period. According to Peller, this is the result of healthier bringing up and the increased care given the children of the masses in the last few years. In 1932 adolescents were better developed in both height and weight than in 1929 to 1931. Despite the extent of the investigation, Peller believes that this conclusion is the result of some error. The conclusion was not due to the fact that better classes of people were reported on in 1932. The possibility is discussed that famine in the younger years after the war and during the period of inflation influenced development. The greater the time since the period of inflation the nearer are the youths to an optimal stage of development.

The economic depression did not show the slightest influence on the development of Viennese adolescents in 1932. At this time there were, on the whole, no more underdeveloped and underfed children than in the earlier years.

ABT, Chicago.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Cleveland, May 2-4, 1935

Fourth Session

Friday Evening, May 3

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ANTAGONISTIC EFFECTS OF SODIUM AND POTASSIUM SALTS ON BLOOD PRESSURE AND CARBOHYDRATE METABOLISM IN DIABETIC CHILDREN. DR. IRVINE MCQUARRIE and DR. W. H. THOMPSON (by invitation), Minneapolis.

The specific effects of the ingestion of large quantities of sodium and potassium salts on the carbohydrate metabolism and blood pressure have been studied under standard conditions in 1 nondiabetic and 4 diabetic children. The investigation was suggested by the discovery of an elevated blood pressure in a 15 year old diabetic patient who was allowed to eat between 60 and 80 Gm. of sodium chloride daily to satisfy an abnormal craving for salt. When he was placed in the metabolic ward on a standard diabetic regimen with the intake of sodium chloride limited to 1 Gm. for each of his four equal meals and with the dosage of insulin adjusted at such a level as to permit the excretion of between 50 and 70 Gm. of dextrose daily, the systolic blood pressure taken with the patient in the reclining posture was found to vary throughout the day between 108 and 116 mm. of mercury, and the diastolic, between 70 and 80. Following an increase in the allowance of sodium chloride to a total daily intake of 60 Gm., with no other change in the regimen, the arterial pressure was again found to rise after two days to new levels, the systolic pressure ranging between 158 and 174 mm. of mercury, and the diastolic, between 110 and 118. At the same time it was observed that the degree of glycosuria was greatly diminished, the amount excreted during twenty-four hours having dropped from the previous level of between 50 and 70 Gm. to between 10 and 25 Gm. Withdrawal of the added sodium chloride again caused a reversal of the picture; i. e., the blood pressure again fell to the normal levels, while the excretion of dextrose rose to the former high level. Similar observations have been made repeatedly on this patient and also on 3 other diabetic children. One of the latter, who had mild diabetes, required no insulin but responded to variations in the intake of sodium chloride, as did the other 3, who received amounts of insulin throughout the tests. One nondiabetic control subject showed a similar elevation of the blood pressure after taking 40 Gm. of sodium chloride daily, but only when the potassium of the diet was relatively low, as in the special simplified diets given to the diabetic patients.

In comparative studies designed to determine which of the two elements composing the sodium chloride is responsible for the phenomena observed, the effects of other salts containing either sodium or chlorine were investigated. Sodium citrate and sodium bicarbonate were found to have similar but less striking effects. Potassium chloride was found to have directly opposite effects from those of sodium chloride, the blood pressure falling somewhat below the base levels and the degree of glycosuria increasing significantly after a few days' ingestion of from 12 to 30 Gm. When given simultaneously with sodium chloride, potassium chloride was found to offset completely the effects of the sodium chloride when given in one-third equivalent amounts. The effects of other salts are being investigated.

While the blood sugar values during fasting were found to be at lower levels during the periods of a high intake of sodium chloride than during the control

periods, the shapes of the curves for dextrose tolerance were not significantly different. The respiratory quotients during fasting were slightly higher during the periods of a high intake of sodium chloride than during those of a low intake in 2 patients. While more exact interpretation of the phenomena observed must await further investigation, it can be concluded that carbohydrate is utilized more efficiently as a result of the diet high in sodium and low in potassium. The few measurements of the blood volume made on these two patients during the different periods did not show consistent variations, in spite of a gain in body weight of as much as 5 per cent due to retention of water during the periods of the high intake of sodium chloride.

DISCUSSION

Dr. Daniel C. Darrow, New Haven, Conn.: I should like to ask Dr. McQuarrie whether he has observed these effects in all diabetic patients or only in certain diabetic patients.

Dr. Irvine McQuarrie, Minneapolis: The only patients on whom we have carried out this investigation were those whom we could take into the metabolic ward and study carefully, which means that the number of cases has been limited. Whether such a study would be effective in all diabetic patients I do not know. Like data have been obtained from 1 patient with mild diabetes who was not receiving insulin and from 3 others receiving insulin. The same phenomena would probably be observed in the majority of diabetic children under comparable conditions. The effects of sodium on the blood pressure and glycosuria are not obtained unless the intake of potassium is very low.

Progress Studies in Diabetes Mellitus in Childhood. Dr. Julian D. Boyd and Dr. Abraham Kantrow (by invitation), Iowa City.

During the past ten years about 170 children with diabetes mellitus have been treated under a standardized regimen, receiving diets with a fixed ratio of ingredients, designed to meet amply all the nutritional requirements of a normal child and to permit full activity. Each child has been reexamined repeatedly, permitting the collection of copious data pertaining to the progress of the patient and of the disease. As a first approach to the analysis of these data, values are presented pertaining to the initial physique, the type of growth while the child was under treatment and the progressive requirement of insulin exhibited with the continued duration of the disease. Although the present analysis covers only two thirds of the members of the series and the plan of analysis is still experimental, the following conclusions seem valid:

1. Contrary to certain published observations, there is no characteristic overgrowth of diabetic children at the time of onset of their disease.

2. These children as a group grow at a satisfactory rate, tending to approach in both height and weight the average standards used for comparison.

3. The relative requirements of insulin, with due consideration for increased growth and the intake of food during the period of observation, tend to progress steadily throughout childhood; a sudden acceleration is to be noted at the ages of 9 to 11 years, apparently in advance of obviously accelerated growth. This accelerated rate of increase in the requirement of insulin persists until adolescence is well established, following which the required dose appears to become stationary at a lowered level. The data suggest that the effect of other endocrine secretions is of importance in this regard.

4. Evidence exists that standardized methods of treatment of diabetic patients may be employed with advantage and safety to the patient and with convenience to the physician, provided that the regimen meets fully the nutritional requirements of the normal child.

DISCUSSION

Dr. Frank Neff, Kansas City, Mo.: Dr. Boyd is fortunate to be able to follow such a large class of diabetic patients year after year. What I have to

say, however, concerns the diagnosis rather than the progress of the disease, if this is not out of order.

Within a few months I have had the opportunity to see 2 infants, 13 and 4 months old, respectively, both in a coma. One had an acutely enlarged liver, no glycosuria, and hypoglycemia of 0.03 per cent; the 4 month old baby had hyperglycemia and high glycosuria. In both these children it would have hastened and made easier the treatment if by a simple puncture of the heel the peripheral blood had been taken for the microdetermination of dextrose. I wish to ask Dr. Boyd whether in the repeated estimations of sugar in his cases he has found the micromethod satisfactory and advantageous.

Dr. Julian D. Boyd, Iowa City: We have not had the good fortune or, perhaps I should say, misfortune to treat any diabetic patients as young as those described by Dr. Neff. The occurrence of diabetes mellitus in infants is reported in the literature, and probably the condition occurs more frequently than is recognized because of the nonspecific symptomatology at this early age. The mortality rate is definitely higher among our youngest patients, death usually occurring while the child is under home management. The diagnosis as to the cause of death for such children is frequently meningitis, which probably indicates that acidosis and coma have developed and that the true nature of the condition has not been recognized.

We seldom determine the blood sugar level by the gross chemical method. We use the micromethod throughout. This procedure has been used in our clinic for twelve or thirteen years, and we have no reason to doubt its efficacy. Two tenths of a cubic centimeter of blood is used and the determination conducted according to a modification of Folin's method. Estimations are made before breakfast and at intervals of two and four hours after eating.

Clinical Studies in Faulty Calcification. Dr. Francis Scott Smyth, San Francisco.

Enthusiasm for endocrine factors in calcification has led to the consideration of parathyroidectomy for osteoporosis of various types. While recognizing the classic features of parathyroid adenoma, there remain other instances of osteoporosis which, in children at least, might best be considered from a more conservative point of view. The technic of Aub, Albright and Bauer, although open to some criticism, is of value in detecting endogenous factors in calcium and phosphorus metabolism.

Four cases are presented. The first two patients were siblings who showed typical parathyroidism. L. M., the third patient, who had been observed over a period of two and a half years, has typical osteoporosis with probable thyroid demineralization complicated by faulty nutrition and atrophy of disuse. Ligation of the thyroid arteries was done; biopsy of the thyroid showed involution, and one normal parathyroid gland was removed. This patient gained rapidly in weight and made a remarkable improvement on a good general diet with plenty of milk plus viosterol, di-calcium phosphate and physical therapy.

The last patient presents many points of similarity with the boy whose study was reported before this society two years ago. Briefly, this is a case of renal rickets with probable parathyroid involvement of a secondary nature, for which roentgen therapy to the parathyroids (as reported by Merritt and McPeak and Cutler and Owen) is being tried, together with transfusions and an alkaline-ash diet high in calcium and low in phosphorus. After six months of treatment his improvement is encouraging, though it is apparently too early to note any lessened effect on the parathyroids as judged by titer (Hamilton's method).

DISCUSSION

Dr. Julian D. Boyd, Iowa City: In 1929 we reported a case of hyperparathyroidism in a young man who was treated by removal of a parathyroid adenoma. Subsequently the boy made a good recovery. Eighteen months later, osteotomies

were performed to correct the deformities of his legs. These were thoroughly successful. After another interval of many months he returned to the hospital at our request to serve as a control for the metabolic studies that were run during his stage of active hyperparathyroidism. We were greatly surprised to find that the chemical findings had resumed the picture seen before the removal of the adenoma. No clinical symptoms, however, had recurred. Ever since his operation he had been on a diet high in calcium and phosphorus. This may account for his continued apparent health. He has been observed periodically ever since, and symptoms have not appeared, although at all times there has been a marked tendency to a pathologically low level of serum phosphorus and elevation of serum calcium. Through the use of large doses of sodium phosphate these phenomena have been controlled in some measure.

We also have seen several cases in which there were aberrant types of hyperparathyroidism. In one of these there were a tumor of the thyroid gland and chemical findings typical of hyperparathyroidism but no bone lesions other than the destruction of one vertebra. Balance periods showed that this patient was maintaining a positive balance of calcium in spite of the fact that she was excreting almost 0.5 Gm. of calcium daily in the urine. She had always been a great milk drinker, and her intake of milk possibly had protected her against the demineralization of bone. It seems probable that cases of hyperparathyroidism pass undetected because routine examinations of the blood or urine for calcium and phosphorus are not made.

Dr. Francis Scott Smyth, San Francisco: I do not know that there is anything further to add to the discussion. I think that the laboratory may fail to detect very slow processes, which is indicated by the case of the second patient with the osteoporosis. We have seen several interesting cases in which roentgen examination suggests fibrocytic disease. In one case the condition was classic focal osteitis. The other patient has a condition which might suggest that he had had active hyperparathyroidism at one time but which had "burned out," similar to the process which may occur in hyperthyroidism.

There is a great deal to be done, I believe, in the interpretation of the laboratory method. We are attempting to get some idea of variation with children of different ages.

Significance of Individual Variations. Dr. Alfred H. Washburn, Denver.

The diagnosis of disease early in its course represents one of the important and ever-present problems in the practice of pediatrics. To tell where the healthy state ends and the pathologic begins is often difficult and sometimes impossible. This fact has served as a stimulus to the setting up of so-called normal standards. For example, one must know the normal weight for a child of a given age and height before one can tell whether the weight of a particular child is normal or not. But what is meant by normal?

Average is not an adequate synonym for normal in this situation. One does not care whether the weight of the particular child coincides with the average of the weights of so many thousand other children or not. What one does wish to know is whether it is within the limits of health for this individual child. Thus it is apparent that the so-called normal standards must be arranged so as to show the limits of possible variation in healthy children as distinguished from those variations, either above or below the average line, which point to the presence of disorder. Eventually one would like to know also the narrower limits of variation for the particular child within the larger zone of differences for all children.

The chief purpose of this paper is to suggest something of the amount and character of the variations which may be found between equally healthy children during the course of painstaking and prolonged follow-up studies which include the checking of many structures and functions. This is done by means of slides which depict the differences in such varied structures as the jaws and hearts or

in such different functions as may be illustrated by leukocyte counts and basal metabolic tests.

The longitudinal type of study of the whole individual child, from birth to maturity, is suggested as a logical method for building up this picture of the zones within which variations in structure or function may occur without indicating the presence of disease.

DISCUSSION

Dr. Harold C. Stuart, Boston: A number of papers at this meeting have dealt with studies of large groups of children, and I am glad that Dr. Washburn has brought out problems of interest in connection with the study of individual children. Dr. Washburn has said that there is little information as to the significance of the individual variations which are found. It seems to me that the reason there is so little material on this subject is not difficult to find.

It is true that pediatricians are in the habit of noting gross individual differences and recognizing types of individuals and that they modify their advice as to care and management on the basis of the type of child with whom they are dealing. But they have not been in the habit of recording differences which they believe fall within the normal range. If they can convince themselves that pathologic changes are not involved in one respect or another, the finding falls within the normal and deserves no further attention.

If in teaching one gives a student a well child, for example, a boy 3 years of age, and asks that he examine him and report later, he will say that he finds nothing in the examination, meaning, of course, that he finds no pathologic condition. If one gives him another boy of 3 years, he may make exactly the same report; and still the 2 boys may be exceedingly different. If one takes ordinary roentgenograms of children of the same age and sends them to a roentgenologist, he will probably send them back with a statement that no pathologic condition is found. Yet if one takes the individual films and compares them, as Dr. Washburn has done, one can notice a great deal of difference.

We have found that if we ask a student to forget for a moment the distinction between the pathologic and normal, take the same 2 boys referred to, examine them together and describe the differences, it is interesting to note how quickly the student becomes interested.

I believe that if one changed one's point of view and tried to describe what one observes and to compare these findings with the history one would find that many individual differences have unsuspected significance. If one goes into the history of the 2 boys referred to one finds an entirely different set of past experiences. One may find that they react to the same environment in different ways. The significance of many differences is not known, because there has been no opportunity to compare data in this way, as no systematic record has been kept.

I wish particularly to suggest this method of teaching medical students the physical examination of the child. I am convinced that if students are asked to examine normal children or those with all the findings falling within the range of the normal, with the sole purpose of finding pathologic changes, the physical examination will be very much more useful and interesting to them.

Dr. Joseph Brennemann, Chicago: I have never been very much interested in weight, charts and tables. I am one of the few physicians who have never had these on the wall of my office. I do not think that one can express those findings in terms of one thing or even in terms of a small broad curve. Adults vary a great deal. Dr. Washburn and I are probably equally healthy, and yet there is considerable difference in our general bodily architecture. I do not know but that insurance companies would look rather askance at both of us from exactly opposite views. Children vary normally in the same way.

I think that all of us have suffered a great deal in the past from roentgen interpretations not only as to hilar shadows but also as to a varying size of the heart. We have all seen thymus glands that were broad before treatment, if the

roentgenogram was taken during expiration, appear narrow after treatment, if the roentgenogram was taken during inspiration.

I have been interested in Dr. Washburn's work because I think that it is along the right line. He is trying to find the limits of the normal. I do not know whether he can make such limits broad enough, but I hope that when he makes graphs or curves that tell what the normal is and what the upper and lower limits are, he will make them broad, and I doubt very much whether then they will be broad enough.

Dr. Fritz B. Talbot, Boston: It is fortunate that Dr. Washburn is doing this work.

I followed the work with a great deal of interest. One thing that impresses me most is the differentiation that Dr. Washburn is making between the average and the spread of the normal. I think that all medical students are taught the average, and they ought not to be taught the average; they ought to be taught extremes of the normal. The reason they have not been taught the extremes is because they have not been known. Dr. Washburn is helping answer a great many of these questions.

It is peculiarly fortunate, too, that this work, which is entering many fields, is being carried out on the same children or group of children. In other words, the work is not based on standards for the heart in one group of children in San Francisco, standards of metabolism in Florida, standards of the pulse rate in Chicago and so forth. All the standards are determined on one group of children. In my mind, that is what is making this work so important.

I should like to ask Dr. Washburn not to complicate these figures and increase the error by dividing the total calories by the body surface, weight or height, but to record the total calories in every instance.

Dr. Alfred H. Washburn, Denver: I am grateful to Dr. Stuart, Dr. Talbot and Dr. Brennemann for this discussion. I have nothing to say except to answer the last question which Dr. Talbot raised.

I am not personally responsible for the work on metabolism, which is being done by Dr. Robert Lewis, the biochemist, and Miss Kinsman. They wished me to use the chart that referred to weight or height rather than my own. In their preliminary report, which will be made in the near future, the results will be charted by all the various methods so that comparison with other published reports may be easily made.

The Meaning of an Average. Dr. A. A. Weech, New York.

The purpose of the speaker was to describe the methods which have been developed by the statistician for treating an average and to point out how, in the analysis of biologic data, the methods can be utilized to yield the maximum of precise information. Definitions were given of the arithmetic mean, the median and the mode, and an approximate formula was presented for obtaining the value of the mode. By illustration the technic of arranging data in a polygon showing frequency was portrayed, and the meaning of a normal distribution was discussed. In connection with the normal distribution a description was given of the standard deviation from the mean as the accepted method for expressing range in a series of measurements. The accuracy or reproducibility of an average was defined in terms of its probable error, and it was shown that two averages can be compared in such a way as to allow for chance variation by utilizing the probable error of their difference. Finally, the necessity for caution in applying the usual statistical formulas to asymmetrically distributed data was emphasized.

DISCUSSION

Dr. Alfred H. Washburn, Denver: When Dr. Weech and I received the program for this meeting, we were both somewhat exercised over the idea that we might be talking about the same thing, when we read the two titles side by side. Fortunately, quite obviously, we are not.

I wish to say a few things about Dr. Weech's paper. I think, in the first place, that he did the Society a real service by stimulating interest in a more wise and careful use of statistics. I shall have to confess that up to a few years ago I understood so little about statistics that when I undertook my present work I was obliged to spend my evenings taking an evening course in statistics in the University of Denver. I found that necessary even to understand the literature in certain fields.

Granted that my knowledge is far behind Dr. Weech's, I feel justified in saying that he might have been more frank or more vehement in his denunciation of the unwise and erroneous use of statistical methods. I feel that one should either learn to use them correctly or avoid their use.

I have seen many persons with a smattering idea of statistics trying to use them. Certainly the wise use of statistics often helps in clarifying certain findings or bringing out interesting correlations between groups of findings. But one must be sure of two things before resorting to statistical methods: first, that the original data are accurate, well checked and adequately controlled before one resorts to modern statistical analysis; second, that there is a sufficient volume of data to enable one to portray the entire zone of variation which one wishes to portray. I am tempted also to add that this method does not portray the individual characteristics which are possessed by some one child.

Fifth Session

Saturday Morning, May 4

How Far Can the Pediatrician Go in Mental Hygiene? Dr. Bronson Crothers, Boston.

The present situation in regard to mental hygiene activities of pediatricians is thoroughly absurd. A great deal of the difficulty is that there is a general assumption that there is a "whole child" or rather a series of such children for whom the pediatrician is responsible. Every one seems to think, in controversial moments, that the whole child should be supervised by some single expert. In ordinary life no sane person makes any such assumption. The distribution of the control of the child between different persons and the abolition of control by adults for a great share of the time are the routine procedure of all sensible parents.

The only way to get very far seems to me to be to work out some general formula which will indicate the special responsibilities of the pediatrician. If one wishes to be conventional, one might try to work out a pediatric whole child, but that would leave one open to attack by those whose own whole child overlapped.

The simpler method is to try to find out ways in which one can develop a specific pediatric art of medicine. I think that all pediatricians have accepted the idea of growth and development, and they have also accepted responsibility for the supervision of well children. In addition, they have undertaken to give prompt and adequate service to sick children. Nothing can be safely added to pediatrics which renders the practitioner unavailable for the care of sick children, no matter how desirable the new technic or procedure may be.

With this reservation in mind, the opportunities offered to pediatricians can be considered.

1. Physical growth and development are obviously manageable, and adequate teaching of these subjects is obligatory.

2. Intellectual development is, and I think should be, the particular province of the psychologist working with teachers. However, the pediatrician should be aware of the work being done and should be able to deal competently with outspoken deviations. On the whole, the relationship between psychology and pediatrics seems to be simple and practicable, but I do not think that physicians are ready to take over psychology.

3. Personality study of the patient is obviously the essence of the effective art of medicine, and persistent efforts should be made to become adept at it, but no method of study which prevents the pediatrician from giving prompt attention to patients with physical disease is admissible. The meticulous keeping of the time-consuming appointments is one of the difficult things to arrange. For this reason alone the prolonged interviews of the conventional psychoanalytic schools are almost impossible.

4. Familial relationships are of vast importance, but it seems to me clear that no pediatrician should allow himself to be maneuvered into a position where he undertakes to be responsible for the actual treatment of adult members of a family. This reservation, if accepted, makes "attitude therapy" an improper technic for the general pediatrician.

It seems to me evident that the pediatrician should be completely aware of the educational and emotional implications of his medical care of patients and should also be responsible for dealing with deviations from ordinary standards of growth and development. This is a large order, and perhaps it is all that he can do. When he gets beyond this field he should recognize the superior sophistication of teachers, psychologists and psychiatrists. Naturally there is no possible objection to acquiring on top of pediatric training a real competence in another field, but it is absurd to assume that pediatric training is, or necessarily should be, sufficient to enable physicians to deal with all the problems involved in bringing up children.

DISCUSSION

DR. HERBERT B. WILCOX, New York: Not long ago a psychiatrist who may well be called pediatric-minded stated that in a review of 250 cases under her own observation, compared with an equal number taken from several clinics, one common factor, that of parental mismanagement, appeared in all. Her experience led to the question, "Is there, from a psychiatric standpoint, such a thing as normal child-parent relationship?"

In the assay of the status of any well child, care must be taken to bring out the general background—the heritage plus environment and control, the example offered for imitation, and the influences conditioning the child's early imitativeness and acquirement of standards. It is fair to assume that there is some relation between early behavior problems and later mental disturbances of a more serious nature. If this is so, it is obvious that the pediatrician has a peculiar opportunity in the prevention or modification of such conditions. He is plainly obligated to so inform himself as to the psychiatric aspects of child care as to be able to avoid the results of unwise control—to be able intelligently to cooperate with the psychiatrist when necessary, or perhaps avoid this necessity by his own ability to recognize early and handle properly these conditions as they arise.

As teachers pediatricians should see to it that their students are made psychiatric-minded and as interested in the control and management of the physically well child as they are in the child suffering from organic disturbance.

Today patients are being admitted to hospitals for the care of mental disease in greater number than the corresponding increase in population warrants. One half the hospital beds in the country are now occupied by persons with mental disorders. It is estimated that since 1930 1,000,000,000 patients have lived out their lives uselessly and unhappily in institutions for the care of mental disease and that a large number are being cared for at home at great cost to the efficiency of members of their own families.

A psychiatrist of note has stated that perhaps one half of the enormous toll of the youth of this country taken by mental disease could be avoided by the application in early childhood of the information and resources now available. It is true that too many have to wait until the condition is advanced enough to warrant their commitment to an institution before adequate treatment can be obtained.

As to the question whether any one physician can assume responsibility for the whole child, one wonders why the exception should be made of these functional

disturbances. Perhaps the prevalence today of the milder forms of mental unbalance in childhood and later life is due largely to the fact that the child's mental health has been to a great extent neglected by the pediatrician in the past. It is difficult to understand why functional disturbances of the central nervous system should be considered outside the responsibility of the pediatrician any more than those of any other bodily system.

How far should the pediatrician go in the matter of psychiatric care? Far enough at least to recognize the possible connection between the early phobias, tics, neuroses and the later-appearing dementia praecox, manic-depressive psychoses and other similar disturbances; far enough to put his teaching of the management and training of the child on a par with the diagnosis of organic lesions; far enough, too, to have a definite opinion as to whether or not psychoanalytic methods can be applied in the first decade without causing introspection and aggravating conditions that already exist, and certainly far enough to appreciate that the psychoneuroses of childhood may be evaluated and successfully managed without resort to psychoanalytic methods in most instances.

If pediatrics can be called internal medicine applied to the period of growth, training, conditioning and education, the pediatrician should be prepared to meet such temperamental difficulties as are associated with this period. These are naturally aggravated by the dominance of receptivity over expression and occur at a time when outlets are early limited by natural causes and frequently further inhibited by unnatural parental restraint.

In order that pediatrics may function in this way the pediatrician must have and be capable of imparting to his students definite psychiatric knowledge, together with an appreciation of its limitations, if it is to be safely applied to the early months or years.

Dr. Horton Casparis, Nashville, Tenn.: I think that all pediatricians, in their attempts to prevent, diagnose and treat physical disease, recognize that there is an indissociable integration of the mental and physical functions of man. They always subconsciously know that these two functions cannot be separated, but it seems to me that it falls to them to make a conscious effort to assume the responsibility for the whole child or, in other words, for his equally important mental and physical health. I use the term mental health advisedly, because I believe that it is important to place the child's behavior on the same plane as physical health if one expects to get general recognition of its everyday importance.

This does not mean that the pediatrician does not call on the psychiatrist or others qualified whenever assistance is needed in the matter of mental health, just as he does not fail to call on the surgeon and dentist when help for the child is needed in those fields.

As important as we know prevention to be in physical disease, it is equally or more important in the realm of mental ill health. Prevention, to be most effective, must begin at the beginning, and we as pediatricians, since we have access to children from the beginning, have above all others an excellent opportunity to assume responsibility for this phase of work. If we familiarize ourselves with the subject it will be seen that the elemental beginnings of behavior difficulties are easily recognized and are about as definite as are beginnings of physical disorder. In the young infant trends which, if let alone, become the components of behavior problems later are usually definite and clearcut, and indications for their prevention are also definite. Accomplishment is frequently difficult because of poor parental material with which to work.

It seems to me, then, that if we assume this reponsibility for the whole child, and I think that we should, we can help greatly in teaching to laymen, nurses, medical students and physicians the everyday common sense principles and practices by which persons learn to live adequately.

Dr. Bronson Crothers, Boston: I think that Dr. Wilcox and Dr. Casparis are taking for granted a certain amount of evidence which I do not believe exists. I doubt whether any psychiatrist could be shown a group of patients and say,

"I could have cured 50 per cent of these patients." Psychiatrists said that twenty years ago when the mental hygiene movement was in full flower and when there was much propaganda along that line. One would hear psychiatrist after psychiatrist give the figures and say, "Prevention would have been possible in 50 per cent of these committed people." I do not know of a single practicing psychiatrist today who would make that statement. I emphasize the words "practicing psychiatrist."

I do not believe that it is going to be simple to find out these cases, isolate them, going back over dementia praecox and so forth, and say that one finds this pattern straight back. When Dr. Washburn and Dr. Lucas bring their cases up through, I believe that they will find that they are not good "pickers" relative to the child who will show mental abnormality.

Furthermore, the attitude which Dr. Wilcox takes, for which I have the greatest sympathy and respect, is very dangerous unless one is right.

One may say to a mother, "I have chosen your child for the prevention of mental disease; if you carry out my orders he will be all right." After ten years a crack may come, and she goes back and says, "I failed. It is my fault that he is incompetent." The sense of appalling guilt that failure to prevent a preventable disease brings on is one of the greatest dangers of the mental hygiene movement.

I do not believe that we are at present equipped to deal with this problem on the basis of the prevention of mental disease. Psychiatrists have not shown us how and, if they know, they have not given us dilution or selection of knowledge which makes us act effectively in that regard.

The question which Dr. Casparis brings up is another matter. He still believes in the whole child as the province which the pediatrician should control. He believes that mental disease is analogous to physical disease and that expertness in dealing with physical disease carries with it the ability to deal with mental disease on exactly the same basis. I think that this is an exaggeration.

As pediatricians are trained, or even as psychiatrists are trained, the teachers, the psychologists, the social workers and others are involved in this. I do not believe that bringing up a child is a medical problem alone. It happens that the physician is about the only one who can be called in on a per diem arrangement. He is the only one to whom one can go and pay a fee for an isolated piece of advice. One pays the teacher by the year or through taxes.

A great many persons have believed that the way to carry on mental hygiene is through the schools. The physicians and the schools should work together on this problem, and each should know what the other is doing; largely, that is not done.

If one could get in medicine, in the training of pediatricians, a really good working knowledge of how children are brought up and what happens to them when education is interfered with, the bearings of disease in terms of education and so forth, I think that one would be getting to a basis where one could really talk thoroughgoing pediatric knowledge. As it is now, I have heard psychiatrists say, "Mental disease is like tuberculosis." Persons who talk like that may be good psychiatrists, but they do not know anything about tuberculosis.

The notion that there is a situation in which physicians are dealing with incipient mental disease and are preventing 50 per cent of the cases, if they are right, dooms us all to frustration.

IMPORTANCE OF THE STANDARDIZATION OF ALLERGIC ANTIGENS (ALLERGENS) FOR DETERMINING SKIN SENSITIVITY BY THE INTRADERMAL METHOD. DR. D. MURRAY COWIE and EMMA WARDELL, PH.D., Ann Arbor, Mich. (by invitation).

Some national and international method of standardization of allergen extracts or emulsion seems necessary. Since our first report (AM. J. DIS. CHILD. **49**:1384 [May] 1935) we have made further observations. We determined the nitrogen content of 137 extracts of allergens (1:100 by weight) prepared by reputable manufacturers and commonly used in skin testing. There is a wide variation in the nitrogen content. In this series it varied from 122 mg. per hundred cubic centimeters

to 1.6 mg. A 50 mg. allergen extract gives a larger and more pronounced skin reaction in a given case than a weaker extract (0.05 mg.) of the same allergen. We found that these 137 allergen extracts when brought to a nitrogen value of 0.05 mg. per hundred cubic centimeters give very satisfactory and more comparable reactions. It is suggested that the nitrogen value may be lowered still further. Observations are in progress.

The nitrogen value was selected as a standardizing measure not because the allergen is a nitrogenous substance but simply because the nitrogen value is a constant and fairly easily determinable factor in all extracts. Should the extract be a protein, a polysaccharide or any other substance, varying the nitrogen content varies all the constituents in the same proportion. This method has been the most generally acceptable.

It was shown that different lots or batches of the same allergen received from manufacturers at different times are frequently subject to wide variations in their nitrogen content. A difference of as much as 9.3 mg. per hundred cubic centimeters was noted. This was particularly true of old tuberculin diluted 1:10. A batch received in September had a nitrogen value of 0.81 mg. per cubic centimeter. A new batch from the same manufacturer in January had a nitrogen value of 2.5635 mg. per cubic centimeter. It is readily seen how different results may be obtained by intradermal testing with these 2 solutions.

The amounts of active principle extracted by different methods vary markedly. This is another argument in favor of standardization.

Analyses of a number of allergen extracts that have been in use in the clinic for as long as three years and which are still active have shown nitrogen values of from 15 to 9 mg. per hundred cubic centimeters. Allergens uncorked and subjected to varying conditions, such as refrigeration, refrigeration alternating with room temperature and constant room temperature have shown little change in the nitrogen content during a period of three months.

It is suggested that an effort be made to have a standard allergen strength adopted for all allergens used for intradermal testing, including tuberculin. It is thought that quantitative testing may lead to better interpretation of the state of sensitivity and to the determination of whether an allergen is really responsible for the clinical disturbance.

ANTISTREPTOLYSIN TITER IN ACUTE GLOMERULONEPHRITIS. DR. JOHN D. LYTTLE, DR. DAVID SEEGAL (by invitation), and ELIZABETH JOST, B.S. (by invitation), New York.

Todd and Coburn and Pauli have published reports on the antistreptolysin titers of serums from normal persons, from patients having an infection known to be due to Streptococcus haemolyticus and from patients with infection due to other organisms. They showed high amounts of antistreptolysin in persons recovering from infections due to Str. haemolyticus and normal amounts of the antibody in normal persons and those recovering from other infections. In the acute stages of infection due to Str. haemolyticus the antistreptolysin titer does not rise. Todd has described the antihemolysin titers of the serums by recording the reciprocals of the fractions of the neutralizing doses of the serums as units; thus, if it takes 0.01 cc. of serum to neutralize 2.5 minimal hemolytic doses of streptococcic hemolysin, this is equivalent to 100 units of antistreptolysin. Todd considers this value—100 units—the upper limit of normal in the serums of healthy persons without preceding infection by Str. haemolyticus.

In 1933 was reported the antistreptolysin titers of the serums from 22 unselected patients, chiefly children with acute glomerulonephritis. These were single determinations from the sixth to the fifty-seventh day after the onset of nephritis. Twenty of the 22 serums in this group of cases had each a sufficiently high antistreptolysin titer to indicate a recent infection by Str. haemolyticus. Continuing this work, we are presenting now serial determinations in 36 consecutive cases of acute glomerulonephritis for a period of six months after the onset of nephritis.

A study of the figures shows that a majority of the patients had a high titer of antistreptolysin at some time in the acute stage of the nephritis, and that as the nephritis subsided or healed the titer fell to normal. We were unable to show any close relationship between the time of the appearance of this antibody and the development of the nephritis or between the titer of the streptolysin and the severity of the nephritis. It is interesting to observe that in the older age group, while the majority of the patients showed a significant increase in streptolysin titer, the peaks were not as high as in the young children, although the type and severity of the infection were approximately the same as in the younger group. This is unlike the findings reported for other persons with infection due to Str. haemolyticus. Our data show that the medium high figure for all ages is 333 units; for those over 18 years of age it is 166 units, and for those under 18 it is 500 units. However, our series is too small to enable one to draw any conclusions.

We think that a high titer of antistreptolysin in a patient's serum is a specific indication of infection by hemolytic streptococcus. The majority of our patients showed a high titer of antistreptolysin, and we conclude that this is strong objective evidence that acute glomerulonephritis is related to a preceding infection by hemolytic streptococcus. This is our only conclusion. It is interesting to speculate as to the relation of antibody formation and prognosis (for chronicity) in persons with nephritis. The data obtained from a study of children alone can yield little information on this point, since few children have chronic nephritis. The combined study carried out here may eventually throw some light on the peculiar differences between children and adults with respect to the development of chronic nephritis.

DISCUSSION

Dr. Samuel Z. Levine, Flushing, N. Y.: I should like to ask Dr. Lyttle two questions.

In view of the known variations in the antistreptolysin titer of normal persons at different age periods and different seasons, were a series of controls run on parallel age groups in the absence of nephritis?

Were cultures taken from the throat simultaneously with the serial determinations of the antistreptolysin titer of the blood rather than merely an initial culture from the throat, if one was taken?

I did not understand what criteria were employed for diagnosing the presence of streptococcic infections in the nephritic group.

Dr. Max Seham, Minneapolis: We studied a number of children two years ago, using the strain from Clausen's vaccine, a strain extracted from a patient with rheumatic fever. We obtained the following figures: In a group of 26 normal children we found the average titer to be 1:150. In a group of 55 children with a condition diagnosed as muscular rheumatism we found the average titer to be 1:1,500. In children who had just left the hospital after having had an attack of rheumatic fever, in all of whom the disease was inactive clinically, the average titer was 1:1,640. In terms of frequency, 90 per cent of the titers of normal children were 1:200 or less. Only 7 per cent of the titers of those with muscular pains and 11 per cent of the titers of patients with rheumatic fever were 1:200 or less. I wonder whether the contrast shown between the normal and abnormal groups is significant enough to be used for differential diagnosis.

Dr. John D. Lyttle, New York: In answer to Dr. Levine's question, cultures were not taken serially each time that the antistreptolysin was determined. At the onset of nephritis, cultures were taken from the throat and any focus that was active (the ears or the sinuses). Later in the course, cultures were taken if there was any exacerbation of the infection or if a complication such as mastoiditis or cervical adenitis with an abscess developed. For our controls we used the figures of Coburn for a group of student nurses carefully followed clinically and bacteriologically throughout the year and the data for a group of normal persons of different ages studied by Dr. Seegal in New Orleans.

THE SERUM LIPIDS IN REFRACTORY INFANTILE ECZEMA. DR. ARILD E. HANSEN (by invitation), New Haven, Conn.

Studies of the serum lipids in eczema indicate that a low degree of unsaturation of the serum fatty acids exists. Such factors as age, character of the diet and ingestion of food do not seem to bear any relation to these findings. Patients with asthma and hay fever had essentially normal iodine numbers of the serum fatty acids, while those with eczema in addition tended to have low values. The iodine numbers were found to return to essentially normal levels when oils rich in unsaturated fatty acid were administered internally. Coincidentally clinical improvement occurred in many instances. It was found in a few observations that the serum lipid iodine numbers tended to increase when tar was applied therapeutically. The interpretation of these findings is not manifest. However, they indicate that further study of the metabolism of the unsaturated fatty acids may help one to understand better the complex problem of eczema.

DISCUSSION

DR. L. EMMETT HOLT JR., Baltimore: Dr. Hansen is to be congratulated for opening up a new line of attack on the problem of eczema. I am sure that his observations will stimulate a great deal of valuable work. He is also to be commended for the guarded way in which he has drawn his conclusions.

I have no reason to doubt the beneficial effects of this particular treatment. I have had no experience with it. But it seems to me that before one can accept the interpretation that is offered certain other possibilities ought to be ruled out. For instance, the benefit reported may have been due not to particular fatty acids, but to the fact that the intake of fat as a whole was increased. A number of observations are reported in the literature in which improvement in various allergic disorders—particularly eczema and asthma—has followed an increase in the fat of the diet. We recently had a striking example of such a response. When a normal infant was fed a fat-free diet eczema and asthma promptly developed. When fat was restored to the diet (it was butter fat, not a highly unsaturated fat) the allergic manifestations cleared up at once. The observation was repeated; when the fat was withdrawn a second time the symptoms recurred and disappeared as promptly when it was again supplied.

I am inclined to question the significance of the relation between the rise in the blood lipids and the cure of the eczema. If observations on the blood lipids had been made at shorter intervals after the administration of the unsaturated fats I wonder whether the parallelism between the rise of the iodine value and the cure of the eczema would have been so striking. It is known that the oral administration of a highly unsaturated fat causes a rise within a few hours in the iodine value of the milk fat. A few observations which we have made have shown that the iodine value of the blood fat rises just as promptly. I should like to ask Dr. Hansen whether he has made any observations on the blood lipids a few hours after the administration of unsaturated fat. The rise in the iodine value of the blood lipids may be a direct consequence of the diet, quite unrelated to the eczema.

DR. FREDERIC W. SCHLUTZ, Chicago: It must be gratifying to many of the older members, particularly those who worked under Czerny, that this splendid piece of investigative work of Dr. Hansen is substantiating a clinical hunch which this outstanding clinician had many years ago with reference to the unfavorable effect of fat in cases of eczema.

I should like to ask Dr. Hansen whether he has determined the effect of other local applications besides tar. We have had the experience that sometimes the dietary factor alone is rather disappointing and not as certain to be effective as when some local therapeutic agent, such as tar or some other substance, is added. Then the effect is often very favorable.

DR. D. MURRAY COWIE, Ann Arbor, Mich.: I should like to congratulate Dr. Hansen on this splendid piece of work and report a case that may be of interest.

I notice from Dr. Hansen's charts that the patients with hay fever and asthma without eczema did not show a lowering of the unsaturated fatty acid, but that when eczema occurred during the course of or closely associated with asthma the unsaturated fatty acid was lowered. We have recently had in our clinic for the treatment of sensitization a patient with marked generalized urticaria which we were unable to control by the methods that we usually employ. This 7 year old child had eczema at 3 months of age and asthma at 2 years and intermittently since then. He had recently been having alternate attacks of asthma and urticaria, that is, never asthma when urticaria was present. I was interested to see whether sensitized patients with cutaneous conditions other than eczema would respond to the oil treatment in the same way. We did not determine the iodine value in this case. Within twenty hours after the raw linseed oil was given (3 teaspoonfuls a day) the urticaria disappeared. The result was dramatic. However, in the course of several days the urticaria returned.

SUBSEQUENT NOTE.—We then doubled the amount of oil. The urticaria cleared for about two weeks; then it returned again. We discontinued the oil at this time. The patient has remained generally improved, but there have been occasional recurrences of the urticaria.

DR. ARILD E. HANSEN, New Haven, Conn.: Dr. Holt's point that the beneficial results may be a question of the intake of fat as a whole may be well taken. His splendid work, which all the members have probably read, showing that the unsaturated fatty acids and short chain fatty acids tend to be more completely absorbed from the intestine than others is probably significant. It may be that when unsaturated fatty acids are given they are completely absorbed; thus the results may be due to the metabolism of the fat as a whole.

The observations on the fat-free diet were interesting. We placed a patient on a fat-free diet and kept him on this diet for a period of six months. Although he had a decrease in the iodine value of the serum lipids, no cutaneous symptoms developed. We have a report from von Gröer in 1919, who kept 2 infants on a fat-free diet over a long period. One showed a marked exudative diathesis, and the symptoms disappeared when the normal diet was resumed.

We have not observed the blood lipids during the use of any kind of therapy other than general measures, such as trying to prevent scratching, the local use of oil and avoiding contact with water, wool and silk. We do not believe that the usual form of therapy should be on such a basis as we have outlined in this study. However, there are a certain number of instances in which, in addition to the other therapeutic measures used, the use of corn oil or linseed oil may help to control otherwise intractable eczema.

As to our experience with the blood lipids in urticaria, we have had none. We found some adults who had otherwise intractable forms of cutaneous eruption over a great many years who in a relatively short time showed a rather remarkable change in their condition and their comfort, as well as disappearance of the eruption, when oils rich in unsaturated fatty acids were given. In other cases, particularly as shown by Cornbleet and his co-workers, there was an indication that many of the patients must be given this therapy over a long period before they are benefited.

As to Dr. Holt's question concerning the length of time that is required to cause the iodine values of the blood lipids to change appreciably, we may mention that the shortest time in which we have seen this occur is about two weeks. In some experimental work now being done in cooperation with Dr. Wilson, we have found that dogs on a diet very high in fat had changes in the iodine values after from two to three weeks, when the blood specimens were examined at uniform intervals during fasting. The changes that occurred were in the direction of the degree of unsaturation of the dietary fats. We do not believe that the significance of the changes found in the eczematous infants is the same as that of the changes found during the absorption of fats following a fatty meal.

CELL AND PLASMA LIPIDS IN ANEMIC STATES OF CHILDHOOD. DR. THOMAS B. COOLEY, DR. PEARL LEE (by invitation), BETTY N. ERICKSON, M.A. (by invitation), HELEN STERNBERGER, PH.D. (by invitation), and FRANCES COPE HUMMELL, M.S. (by invitation), Detroit.

This is a part of a projected study of the normal and pathologic chemistry of the red cell, carried out in the Children's Hospital of Detroit and the Research Laboratory of the Children's Fund of Michigan. It was inspired by the obvious lack of definite knowledge on this subject and especially by a belief which we have long cherished that peculiarities in the fundamental structure of the cell play an important part in the pathogenesis of the constitutional hemolytic anemias. First attention was given to the lipids, because there is much to suggest that variation in their total amounts and proportions may be related to susceptibility to various forms of hemolysis and because present methods are more adequate for their study than for that of the portein fraction, which will be investigated later. Findings are presented for the cells and plasma of normal children and of patients with hemolytic icterus, sickle cell anemia and erythroblastic (Mediterranean) anemia, in each of which diseases there is other evidence of peculiar cell structure. The findings for the cells of normal children are fairly constant; those for the plasma vary within a wider range.

The figures given are for the total lipids, the neutral fat, the free cholesterol, the cholesterol esters, the total phosphatides, lecithin and cephalin. In each of the anemias reported on there was an important variation from the normal in some of the constituents of the lipids.

In hemolytic icterus without splenectomy, the general level of the cell lipids, calculated in milligrams per hundred grams of cells, was definitely low, though the cholesterol esters and cephalin were slightly high. Calculated in micromicrograms per cell, however, all the lipids were above the normal range, the reason for this discrepancy being that the cell in this disease is unusually heavy. After splenectomy there was a distinct tendency to a return to normal figures.

Cases of sickle cell anemia in both patients who had had splenectomy and those who had not had splenectomy were studied, also cases of the sickling trait without anemia (sicklemia). Before splenectomy there was marked increase in the total lipids and the total cholesterol and esters with a decrease in lecithin. After splenectomy there was a less complete shift toward the normal than in hemolytic icterus. The patients with sicklemia showed no abnormality except an increase in the cholesterol esters. This would seem to indicate that the property of changing shape must be due to some other cellular constituent than the lipids.

The one patient with erythroblastic anemia at our disposal had splenectomy some years before. Her cells showed much the greatest abnormalities observed in the series—more than twice the normal total lipids and total phosphatides and marked increase in the total fat and free cholesterol, but no esters.

The figures for the plasma show no correlation between the plasma and cell lipids.

Physicochemical studies and studies of the minerals, carried on concomitantly with the studies of the lipids, have not shown anything remarkable.

At this stage we are not justified in hazarding any conclusions as to the part of the lipids in the cell structure.

DISCUSSION

DR. GEORGE M. GUEST, Cincinnati: Having been engaged in a somewhat related study of some of the constituents of the red blood cells which may be observed to change in various conditions, I wish to express my appreciation both of the importance of the studies that Dr. Cooley has reported and of the difficulties inherent in such an investigation. In the past, chemical studies of nutritional disturbances in infants have been confined for the most part to the blood serum and body fluids, and the present knowledge of intracellular chemical changes is scant in comparison with what has been learned of the changes which occur in those fluids. Some of the difficulties encountered in the interpretation of the data obtained

from chemical studies of blood cells deserve emphasis. Because of marked alterations in size of the red cells commonly observed in different types of anemia, any values used to describe the composition of those cells must be related to both the content and the concentration of the substances measured in the cells. When values describing the chemical constituents of the cells are expressed in terms of units (as micromicrograms) of substance per average cell, the changes observed in those values may be due to a change of the cell in size alone. On the other hand, values expressed in terms of concentration (as grams per hundred cubic centimeters of packed cells), if used alone, may not disclose important structural changes in the cells. Values expressed in these two ways may be found to vary independently of each other or in parallel directions, and analysis of the results of such studies as those reported here must be made with both points of view held clearly in mind.

DR. THOMAS B. COOLEY, Detroit: I should like to add, in line with Dr. Guest's remarks, that we have made some discoveries in this study which might have a bearing on some of the common methods of study of the blood, for instance, the remarkable variation in the weight of the cells. In determinations of volume by the hematocrit the heavy cells would, of course, pack much faster, and one might have to consider more carefully than we have the desirability of reducing the volume to an absolute minimum instead of relying on centrifugation at a given rate and time.

Various questions come up from time to time in a study like this which cause us to add to the number of procedures. Not all these are shown on the slides. This is only a very preliminary presentation.

RELATIONSHIP BETWEEN CARBOHYDRATE AND CERTAIN FATIGUE FACTORS. DR. FREDERIC W. SCHLUTZ and ELEANOR BLISH, PH.D. (by invitation), Chicago.

A study of the changes in the acid-base balance and sugar in the blood of children following exercise has been carried out in the department of pediatrics of the University of Chicago on a total of 10 subjects between the ages of 8 and 13 years. An investigation of the influence of the ingestion of different carbohydrates on these factors has also been begun.

The determinations of the acid-base balance were made in the course of each experiment by the microtechnic of Shock and Hastings, which requires but 0.1 cc. of blood for a determination of the p_H of the serum, the carbon dioxide of the whole blood and the cell volume. The blood sugar was determined by the micromethod of Folin on 0.1 cc. of blood. The blood was collected under oil in oxalated tubes from puncture of the finger-tip. Samples were drawn before exercise, after fifteen minutes and thirty minutes, respectively, of exercise and on exhaustion, and one sample was drawn on recovery, from twenty to thirty minutes after exercise.

The exercise consisted of riding a stationary bicycle ergometer. The work done was standardized, so far as possible, for each subject and calculated in watt-hours of work from the records of voltage obtained during the riding and the calibrations of output of the bicycle ergometer.

From the results on the acid-base balance, the carbon dioxide tension and the change in the fixed acid of the blood were calculated. The results on both the acid-base balance and the blood sugar on samples taken during exercise were compared with the results obtained under similar conditions and at similar intervals without exercise.

The sugar given in this series of experiments was cerelose, a pure form of glucose obtained from corn. In most cases 2 Gm. per kilogram of body weight was given in about 250 cc. of lemonade.

The results may be summarized as follows:

In 5 subjects of the 10 studied in this series, the entrance of fixed acid into the blood was inhibited at either the fifteen minute period or at exhaustion, when sugar was given at the beginning of exercise. In 2 cases in which the sugar was

given one-half hour before the exercise was begun, the same decrease in fixed acid was observed, although the results seem to indicate a more marked decrease when the sugar was given at the beginning of exercise.

In all the cases exercise inhibited the rise in the blood sugar at either the fifteen minute period or on exhaustion. In only 2 subjects and only 1 experiment each for 2 other subjects was the lowering of the blood sugar curve (as determined without exercise) delayed until exhaustion. In all the other experiments the curve showed inhibition in the rise in the blood sugar after the fifteen minute period.

The study of the influence of the ingestion of different sugars on the changes in the acid-base balance and sugar during exercise is now in progress. Lactose seems to have no effect in inhibiting the rise in the fixed acid at the fifteen minute interval, as compared with the results obtained during fasting, but shows some tendency to lower it at exhaustion. Fructose and sucrose show no inhibitory effect, and our findings so far seem to indicate that the rise in the fixed acid of the blood due to exercise is greater at either the fifteen minute period or exhaustion after ingestion of these two sugars.

DISCUSSION

Dr. Fritz B. Talbot, Boston: In this connection, in the studies which we made on skin temperature our attention was called particularly to the first three minutes after exercise, in which a significant change takes place in the elimination of heat and perhaps in the production of heat. When Dr. Schlutz carries this work further those first three or four minutes might show some interesting facts.

Dr. W. McKim Marriott, St. Louis: I should like to inquire whether Dr. Schlutz has attempted giving the various sugars without the large amounts of lemon juice; also, if he has tried the effect of lemon juice alone. The absorption of citric acid and the ultimate metabolic conversion of the organic salts to a fixed base would in themselves tend to cause changes in the acid-base equilibrium in the blood.

Dr. Frederic W. Schlutz, Chicago: These are preliminary studies. We need additional data before arriving at far-reaching conclusions. In both the work on animals and these studies on children it was interesting to note that marked changes took place within the first fifteen minutes of exercise and continued in the malnourished child, whereas in the normal subject some adjustment seemed to take place.

In regard to the point brought up by Dr. Marriott, we have not made any check control with reference to the effect of lemon juice. It might be a factor and could possibly influence the results somewhat.

Diagnosis of So-Called Chronic Fatigue. Dr. Max Seham, Minneapolis.

This paper attempts to bring up to date the phase of pediatrics which deals with the diagnosis of chronic fatigue. The methods of diagnosis in use today are physical examination by the physician; determinations of the basal metabolism, blood sugar and calcium content; sugar tolerance tests; the direct method of the psychoanalyst, and the method of case study of the psychiatrist.

To study the value of these methods 240 children who complained of fatigue in the absence of organic disease were selected. The children were studied in the public schools, in the child guidance clinic, in the outpatient department and in private practice. All these children were repeatedly subjected to physical examination. In addition, complete personality studies and blood pressure readings were made on 38, and sugar tolerance tests and blood calcium studies on 14, and 100 were given 16 psychophysiologic tests. Thus all the available methods except psychoanalysis were applied to some of, if not all, the children.

The results of the application of these methods forces one to the conclusion that none of them gives sufficiently comprehensive information to justify its use in diagnosis. The physical examination as employed today assumes a static conception of disease and cannot reveal dynamic changes in the organism. The direct

method of the psychoanalyst and the method of case study of the psychiatrist, valuable as they may be for the diagnosis of grave functional disorders, such as psychoneuroses, are beyond the facilities of the pediatrician. And the psychometric tests, objective though they may be, are unreliable and not valid.

The writer devised a method which will, within the office facilities of the pediatrician, permit one to make a diagnosis not only of chronic fatigue but also of the psychobiologic state of the child. Personal observations of the child in the office, in school, at play and at home were combined with the information obtained by a questionnaire which inquires into the habits of living, the subjective complaints and the changes in behavior observed by the parent and the teacher.

By means of these two methods a composite picture of the signs and symptoms was obtained. These signs and symptoms were grouped as follows: changes in sensation, mentation and emotion [slide 1]; changes in motor activity—hyperactivity, hypo-activity, speech [slide 2]; facial activity and posture [slide 3]; changes in visceral activity and sense organ activity [slide 4].

Objective fatigue, in the sense of a decrease in physical and mental capacity for work, is apparently rare. Hyperactivity is a far more frequent concomitant of feelings of fatigue. The findings indicate that if one adheres to its common meaning fatigue is rare in children; that these children suffer from functional disturbances other than fatigue, for which a common denominator must be chosen by physicians, be it chronic nervousness, hypertension or a new name which would more closely characterize the psychobiologic state of the patient; that if the term chronic fatigue is retained the conception of its meaning will have to change. From the standpoint of the practicing pediatrician, however, the terminology is of minor importance. It is of greater importance that one collect all the information possible which will give the most comprehensive understanding of the psychobiologic status of the child. The combination of the questionnaire submitted to the child and the mother and the observations of the behavior of the child by the examiner offers a satisfactory means for the diagnosis and opens the road for effective treatment of the milder functional disorders in childhood.

DISCUSSION

Dr. A. A. Weech, New York: The methodical manner in which Dr. Seham obtained detailed information concerning the symptomatology in this group of patients is laudable and clear. I do not understand, however, how he evaluates the relative importance of particular symptoms and arrives at a diagnosis. I should like to inquire whether he has encountered any normal children who do not exhibit at least some of the symptoms listed as belonging to the syndrome of chronic fatigue.

Dr. Bronson Crothers, Boston: The paper presented by Dr. Seham, without any regard to details, shows a trend in the field of pediatrics and the mental hygiene movement. He has facts and observations which he made himself. In order to accomplish anything he has to get action and change of routine on the part of the parent and has also to have cooperation of the schools.

All these observations are almost impossible to make in a hospital where the child is put to bed and ordinary behavior is abolished during the period of observation. Undoubtedly Dr. Seham has one series of explanations which are valid only if he is a first rate physician. No psychiatrist who gets a waiver of the physical status before he starts in can accomplish anything with these children.

Dr. Schlutz, Dr. Talbot and any number of others here have indicated over and over a rational way in which the pediatrician can carry weight, not losing his authority over the child, without going too far beyond his actual data. I think that this is where the pediatrician has a logical and fundamental opportunity in mental hygiene work, not through a dilution, as yet unexplained, of adult psychiatry.

Dr. Max Seham, Minneapolis: The reason why I discarded all the other methods with which I started out was because I found them of no practical help

in getting all the information about these children who showed various disturbances that are called functional disorders.

As I studied these children over a long period and under varied circumstances, I noted that I put a disproportionate amount of time and effort into the static methods as compared with the dynamic methods.

I think that all pediatricians spend too much time studying the child with physical methods, but because of limited office facilities or because we have no way of seeing these children in other environments and circumstances we do not attempt to try to understand the dynamic changes, the behavior changes, which these children are undergoing. So I purposely observed some of these children in their homes and was surprised to see how much more information I received by watching all their behavior responses that came up from time to time through the day.

In answer to Dr. Weech's question, I do not think that it is necessary for our purpose to objectify our findings, because I do not advocate these indexes as tests for diagnosis. I present them only as signs to look for in each child. Whether they are found in the normal child or the abnormal child is also irrelevant. They serve one purpose, namely, to enable one to find out all that one can about the individual child.

It is obvious that there are a great many children who are considered adequate from the standpoint of behavior in the broad sense who present some of these signs and symptoms. But in this particular paper I am not interested in the line of demarcation between the so-called normal and abnormal. My interest is in the children who are brought for help who have disorders and maladjustments. What can one find out about them? The most practical part of this scheme, so far as I have been able to use it, is that it helps one in a short time to understand the child as a whole. The method takes about an hour, and one has a listing of all the behavior traits and subjective changes. That list enables one to treat the child more intelligently.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

March 14, 1935

HARRY T. BAKWIN, M.D., *Chairman*

ALEXANDER T. MARTIN, M.D., *Secretary*

THE ANTISTREPTOLYSIN TITER IN ACUTE GLOMERULONEPHRITIS. DR. JOHN D. LYTTLE, DR. DAVID SEEGAL and ELIZABETH JOST, B.S.

Todd and Coburn and Pauli have published the antistreptolysin titer of serums from normal persons, from patients having a known Streptococcus haemolyticus infection and from patients with infection due to other organisms. They showed a high titer of antistreptolysin in persons recovering from Streptococcus haemolyticus infections and normal amounts of the antibody in normal persons and those recovering from other infections. In the acute stages of Streptococcus haemolyticus infection the antistreptolysin titer does not rise. Todd has described the antihemolysin titers of serums by recording the reciprocal of the fractions of the neutralizing doses of the serums as units; thus, if it takes 0.01 cc. of serum to neutralize 2.5 minimal hemolytic doses of streptococcic hemolysin, this is equivalent to 100 units of antistreptolysin. Todd considers this value, 100 units, the upper limit of normal in the serums of healthy persons without preceding Streptococcus haemolyticus infection.

In 1933 we reported the antistreptolysin titer of the serums from twenty-two unselected patients, chiefly children with acute glomerulonephritis—single deter-

minations made from the sixth to the fifty-seventh day after the onset of nephritis. Twenty of the twenty-two serums from these patients contained a sufficiently high antistreptolysin titer to indicate a recent Streptococcus haemolyticus infection. Continuing this work, we are presenting now serial determinations in thirty-six consecutive cases of acute glomerulonephritis for six months after the onset of nephritis. A study of the figures shows that in a majority of the cases a high titer of antistreptolysin developed at some time in the acute stage of the nephritis, and that as the nephritis subsided or healed the titer fell to normal. We were unable to show any close relationship between the time of appearance of this antibody and the development of nephritis or between the titer of streptolysin and the severity of the nephritis. It is interesting to observe that in the older age group while the majority of the patients showed a significant increase in streptolysin titer the peaks are not as high as for the young children, although the type and severity of the infection were approximately the same as in the younger group. This is unlike the findings reported for other persons with Streptococcus haemolyticus infection. Our data show that the median high figure for all ages is 333 units; for those over 18 it is 166 units, and for those under 18 it is 500 units. However, our series is too small to draw any conclusions.

We think that a high titer of antistreptolysin in a patient's serum is a specific indication of infection by the hemolytic streptococcus. The majority of our patients showed a high titer of antistreptolysin, and we conclude that this is strong objective evidence that acute glomerulonephritis is related to a preceding hemolytic streptococcus infection. This is our only conclusion. It is interesting to speculate as to the relation of antibody formation and prognosis (for chronicity) in persons with nephritis. The data obtained from a study of children alone can yield little information on this point, since chronic nephritis develops in few children. The combined study reported here may eventually throw some light on the peculiar differences between children and adults with respect to the development of chronic nephritis.

Book Reviews

Limbs for the Limbless. By John Culbert Faries, Ph.D. Price, $2. Pp. 104, with 12 illustrations. New York: Institute for the Crippled and Disabled, 1934.

This handbook gives to the layman facts regarding the history, construction and use of artificial limbs, which may be helpful to persons in need of them or those who advise the limbless ones and, second, it presents to the surgeon some of the advantages and disadvantages of different kinds of amputation stumps, from the point of view of the maker of artificial limbs.

Better cooperation between the surgeon and the appliance-maker would be of much benefit to the person who has lost a limb, and it is the hope of Faries that a better understanding of the part played by artificial limbs in the economic rehabilitation of the injured and closer cooperation between the surgeon who amputates and the prosthetist who furnishes a substitute for the missing member will be brought about.

The importance of wearing an artificial substitute—especially for the lower limb—is not generally recognized. It eliminates the outward signs of disability, which lessen the prospect of employment; it improves the appearance; it tends to restore one to normal activity and ordinary pursuits, and it permits the body to be borne in the way nature intended it should be.

One-half million amputations of arms and legs resulted from the World War, but in times of peace disease and accidents result in many more. The physical consequences are the disfigurement and the impaired function; the economic dependence on the previous occupation and the patient's ability to adapt himself to another occupation if the necessary limb—arm or leg—has been amputated, and the psychical consequences.

The patient usually is affected more by the loss of the leg than the arm; but this should not be the case, as the amputated leg can be replaced with a much more satisfactory appliance than can be made for the amputated arm.

The historical development of artificial limbs is described from the simple "peg leg" of the prechristian era to the highly cosmetic and mechanically perfect functioning American leg of today. The manufacture of artificial arms has not been as satisfactory, and yet there are some appliances for hooks and other devices which have been of great service to some who have had an arm amputated.

For the best function of a prosthesis ("something added to") the amputation should be made at a point where the appliance can be attached and worn with comfort and so that the remaining muscles can move it to the best advantage.

The American leg is made of well seasoned willow wood, which is light, strong and durable.

If the amputation is through the thigh there are three segments of the artificial leg corresponding to the thigh, shin and foot, with joints at the knee, ankle and toes. The segment which receives the stump is called the bucket. It is carved out inside to fit uniformly over the stump and externally to correspond to the contour of the natural leg.

Children who need artificial legs have been neglected, first, because of the parents' feeling that they cannot afford to supply several limbs during the period of growth; second, because of the awarding of damages to a child as a result of a public accident, the funds being placed in trust till the child is of age, and, third, because of the ignorance of the legal guardians of the physical and psychic results to the child of the failure to provide him with a proper substitute for the missing limb.

The wearer of an artificial limb must remember that it is a tool the effectiveness of which depends on how well he learns to use it. It is important that he learn

to use the artificial leg properly if he is to acquire a natural gait. Of course there are other factors which influence the gait, such as the site of amputation, the length and condition of the stump and the suitability of the appliance.

Proper care must be given to the stump, stump socks and the artificial limb after the choice of the manufacturer has been made. It is unnecessary to say that workmanship and the proper fit are everything in an artificial limb, but to obtain these the person should patronize a limb-maker in his own locality, because the limb should be fitted in the shop.

Part II deals with the points of selection for amputation of the limbs which are most satisfactory for prostheses.

The Effect of Acid, Neutral, and Basic Diets on the Calcium and Phosphorus Metabolism of Dogs. By Agnes Fay Morgan, with the cooperation of the Stomatological Research Group of the University of California. Price, 60 cents. Pp. 106. Berkeley, Calif.: University of California Press, 1934.

This monograph presents in condensed form the summary of a series of carefully controlled observations on the effects of certain variations in the diet on the development of growing animals with especial reference to the bones and teeth.

The results obtained with a standard basal diet composed of purified foodstuffs with a neutral ash were compared with those obtained when the basal diet was varied through the addition of alkali in the form of sodium bicarbonate, acid in the form of ammonium chloride and vitamin D in the form of cod liver oil and when there were variations in the calcium and phosphorus contents. The rate of growth was observed; roentgenograms of the bones were taken frequently, and chemical analysis of the blood and experiments on the metabolism balance were carried out during life. On the completion of the observations histologic studies and chemical analyses were made on the bones and teeth.

The most rapid growth was observed in two groups of animals: those fed alkali diets and those given additional cod liver oil. Of the group fed cod liver oil, those on the alkaline ash diet were found to have less normal bone development than the groups fed the neutral or acid diets, this being interpreted as a result of the accelerated growth. The most severe lesions of rickets were seen in the dogs fed the acid ash diet without vitamin D, and the next most severe in the group fed the alkali ash diets, whereas those receiving the basic neutral diet showed the most nearly normal bones of any group. In dogs receiving a diet low in calcium without cod liver oil the typical lesions of osteitis fibrosa developed, whereas in those receiving diets somewhat higher in calcium, also without vitamin D, osteoporosis or osteomalacia developed. Paradentosis was observed in the group fed the low calcium diet without vitamin D and in all of the dogs fed the alkali diet. Among the animals fed the alkali ash diet there was a distinctly greater incidence of renal damage, as evidenced chiefly by tubular degeneration.

Metabolic balances showed a greater retention of both calcium and phosphorus in the animals fed the alkali and neutral diets than in those fed the acid diet.

In the blood the calcium-phosphorus product was lowest in the dogs fed the acid diet without vitamin D, highest in the group fed the neutral diet and intermediate in the group fed the alkali diet. The blood calcium was slightly lower in the group fed the acid diet. There was no significant change in the percentage of diffusible calcium in the three groups. The inorganic phosphorus of the whole blood was lowest in the dogs fed the acid diet without vitamin D, and the addition of vitamin D raised this level significantly only in this group.

From the observations made it was concluded that diets having an approximately neutral ash produce the most nearly normal physical appearance, bone development, blood composition, calcium and phosphorus retention and bone and tooth ash content. Acid and alkali ash diets accompanied by vitamin D produce the next most favorable results; an alkali ash diet without vitamin D the next best results, and an acid ash diet without vitamin D the least normal results.

The work as a whole is a valuable contribution to present knowledge of the effects of dietary factors on growth and development.

The Doctor's Bill. By Hugh Cabot. Cloth. Price, $3. Pp. 313. New York: Columbia University Press, 1935.

Dr. Cabot begins his book on medical economics by describing the changes that have occurred in the practice of medicine in the past forty years. The first chapters give an account of the developments in this country whereby the change has been made from the family physician to the specialist. The author then discusses in full the various forms of group health services, workmen's compensation acts and forms of health insurance in England and continental Europe. The last part of the book deals with the income of physicians, the ability of patients to pay and some suggested methods of improvement. Cabot does not attempt to enumerate all the possible methods, but weighs the availability of insurance, both national and nongovernmental (by regular life and accident insurance companies), private voluntary plans and methods of private physicians. Compulsory health insurance is discussed in detail. In the final chapters the author examines each of these plans under the following headings: first, doing nothing but attempting to make medical service as good from the standards of education and ethics as possible; second, adopting some plan tried in other countries, and, third, developing a system of our own. This discussion covers compensation acts, voluntary insurance and industrial medicine.

Cabot has done an excellent piece of work in this book. It is a mine of authentic information. He has carefully confined himself to stating the problems without offering a plea for the imposition of any system. It presents to the medical student, as well as to the practicing physician evidences of an economic character and logical comments on the various plans that have been proposed that should enable them to form ideas of their own on this most real problem.

The book is well bound and excellently printed.

The Compleat Pediatrician. By W. C. Davison. Price, $3.75. Durham, N. C.: Duke University Press, 1934.

In this book on pediatrics Davison has worked out an interesting system of cross-indexing symptoms, diseases, treatment and preventive measures. He has omitted no detail of any importance. Although there are many to whom such a method of presentation will not appeal, all may have occasion to appreciate its value as a reference guide. The general index is also very complete.

The chapter headings are:

1. Symptoms and Signs of Disease in Children
2. Diseases, Differential Diagnosis and Treatment
3. Prevention Measures and Child Care
4. Administration of Fluid and Blood to Infants
5. General Suggestions for the Feeding of Normal Infants and Children
6. Drugs and Prescriptions Frequently Used in Pediatrics
7. Laboratory Methods.

Dr. Colwell's Daily Log for Physicians. Price, $6. Champaign, Ill.: Colwell Publishing Company, 1935.

This work describes a convenient method for keeping books for the physician. There are pages at the end for a waiting list for obstetrical records and likewise an annual summary which can be used readily for making out income tax returns. It is an altogether practical book for the physician's desk.

Rapport sur le service des enfants assistés du département de la Seine. Part 2. Pp. 69. Paris: Montévrain, 1934.

This part consists of a complete financial report for 1933 and the proposed budget for 1935.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.
Place: Basle, Switzerland. Time: Sept. 20-21, 1935.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. R. C. Jewesbury, 5, Wimpole St., London, W. 1.
Secretary: Dr. Helen Mackay, 28, John St., London, W. C. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Philadelphia. Time: Oct. 11-12, 1935.
Regions II and III. Place: Hotel Chase, St. Louis. Time: Nov. 18-19, 1935.
Region IV. Place and time not yet decided.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: St. Louis. Time: Sept. 30-Oct. 4, 1935.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Place: St. Louis. Time: Nov. 19-22, 1935.

STATE

Alabama Pediatric Society

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

Arkansas State Pediatric Association

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

Georgia Pediatric Society

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

Indiana State Pediatric Society

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

Louisiana State Pediatric Society

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.
Place: Harrisburg. Time: Sept. 30-Oct. 3, 1935.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. P. McDowell, 142 W. York St., Norfolk.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. C. V. Mulligan, 17 Walmer Rd., N., Toronto.
Secretary: Dr. T. B. Verner, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: College Hall, John B. Murphy Hospital. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Harris County Pediatric Society

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Charles F. Fisher, 756 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April.

CARTOSE

—progress in infant nutrition

It is now two years since Cartose was introduced. Each month larger sales and wider distribution reflect the appreciation and widespread approval of this product by the medical profession.

This maltose-dextrin-dextrose-sucrose carbohydrate for supplementing milk in infant feeding was well established in a remarkably short time.

The success of Cartose is attributed to

(1)—the quality and efficacy of the product
(2)—its reasonable price
(3)—the strictly ethical policy of the company

HIDEX

—we now announce Hidex

A high dextrin (64%) carbohydrate powder with maltose (32%), made by the diastatic conversion of starch

Indicated for those sick and premature babies requiring a slowly digestible and relatively non-fermentable carbohydrate. Hidex, because of its high dextrin content, is not likely to lead to intestinal fermentation and this is an especial advantage in the presence of diarrhea.

SCIENTIFIC SUGARS CO.

Indianapolis, Indiana

FALL * WINTER

Protection

AGAINST VITAMIN DEFICIENCY

Whatever the season, whoever the patient, you know that you can depend on Abbott's Haliver Oil with Viosterol to supply the Vitamins A and D when needed.

For Abbott's Haliver Oil is a highly potent vitamin product . . . therefore small quantities meet the requirements. Each small capsule of Abbott's Haliver Oil with Viosterol is equivalent in Vitamins A and D to not less than four teaspoonfuls of cod liver oil (U.S.P. X, Revised 1934). In small doses of a few drops of liquid—or in perfectly tasteless capsules—Abbott's Haliver Oil with Viosterol relieves your patients of the necessity of taking large, disagreeable tasting doses of other therapeutic agents.

Your patients will appreciate your prescribing a source of vitamins so easily taken. Abbott's Haliver Oil products are stocked by all good prescription pharmacies . . . and sold to your patients at reasonable prices. You may have a physician's free sample by addressing your request to . . . ABBOTT LABORATORIES, North Chicago, Illinois.

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HALIVER OIL

WITH VIOSTEROL

ABBOTT LABORATORIES B 9-55
North Chicago, Illinois

Send me FREE sample of Abbott's Haliver Oil with Viosterol capsules.

_____ M.D.

Address _____

City _____ *State* _____

"THE *amino-acid radicals of bovine milk are somewhat different from those of human milk. In general, it may be stated that the infant requires twice as much of the foreign protein as the protein in human milk in order to satisfy its requirements.*"—*Zahorsky.* Synopsis of Pediatrics.

DRYCO PROVIDES FOR THIS VITAL NEED

THE need for higher protein values in the artificial formula to compensate for biological differences between cow's milk protein and the protein of human milk, is voiced by many authorities. The above quotation is a typical one.

In the weak cow's milk dilutions made necessary by digestive limitations during early infancy, this increased protein need is rarely supplied.

The greater digestibility of Dryco permits feedings that supply ample protein throughout the entire nursing period. Moreover, following Nature's own lead in breast milk, modified Dryco feedings supply their highest protein content during early months when growth is fastest and the protein need greatest.

Simple and concise formula suggestions, based on the foregoing feeding principle, are offered in the Dryco vest-pocket feeding schedule. Copies of this handy guide, for professional use only, will be gladly sent upon receipt of coupon.

THE DRY MILK COMPANY, INC.
350 MADISON AVENUE · NEW YORK, N. Y.

ACCEPTED AMERICAN MEDICAL ASSN. Council on Foods

DRYCO is made from superior quality milk from which part of the butter-fat has been removed, irradiated by the ultra-violet ray, under license by the Wisconsin Alumni Research Foundation (U. S. Pat. No. 1,680,818) and then dried by the "Just" Roller Process.

THE DRY MILK CO., INC., Dept. DCI
350 Madison Ave., N. Y. C.

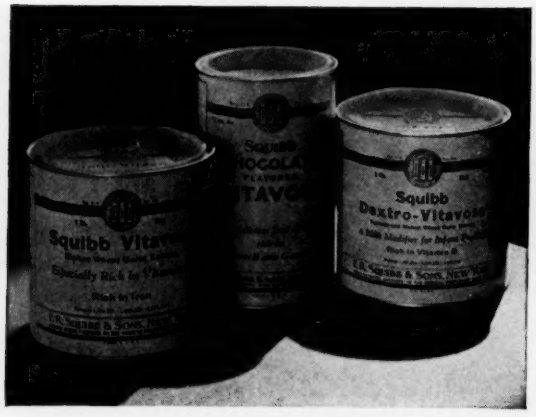
Please send copies of new DRYCO Infant Feeding Schedule.

Name..... *M. D.*

Street.....

City..... *State*.....

Check here to receive samples of DRYCO ☐



MOTHERS · INFANTS · CHILDREN · ADULTS

—all need ample Vitamin B

THE normal Vitamin B requirement of a mother is greatly increased during pregnancy and lactation. The addition of a rich, dependable source of Vitamin B is often necessary to the well-being of both the mother and the infant. This is also true in artificial feeding of infants where milk modification may not supply a sufficient amount of the appetite and growth-promoting factor.

Children, whose appetites are poor, under-par adults and patients on restricted (ketogenic and low residue) diets are frequently benefited by Vitamin B therapy.

Squibb Vitavose Products are exceptionally palatable and dependably potent sources of Vitamin B. They also supply an abundance of Vitamin G (B_2) and assimilable iron salts. There are several Squibb Vitamin B products which may be adapted to the patients' needs.

SQUIBB VITAVOSE PRODUCTS

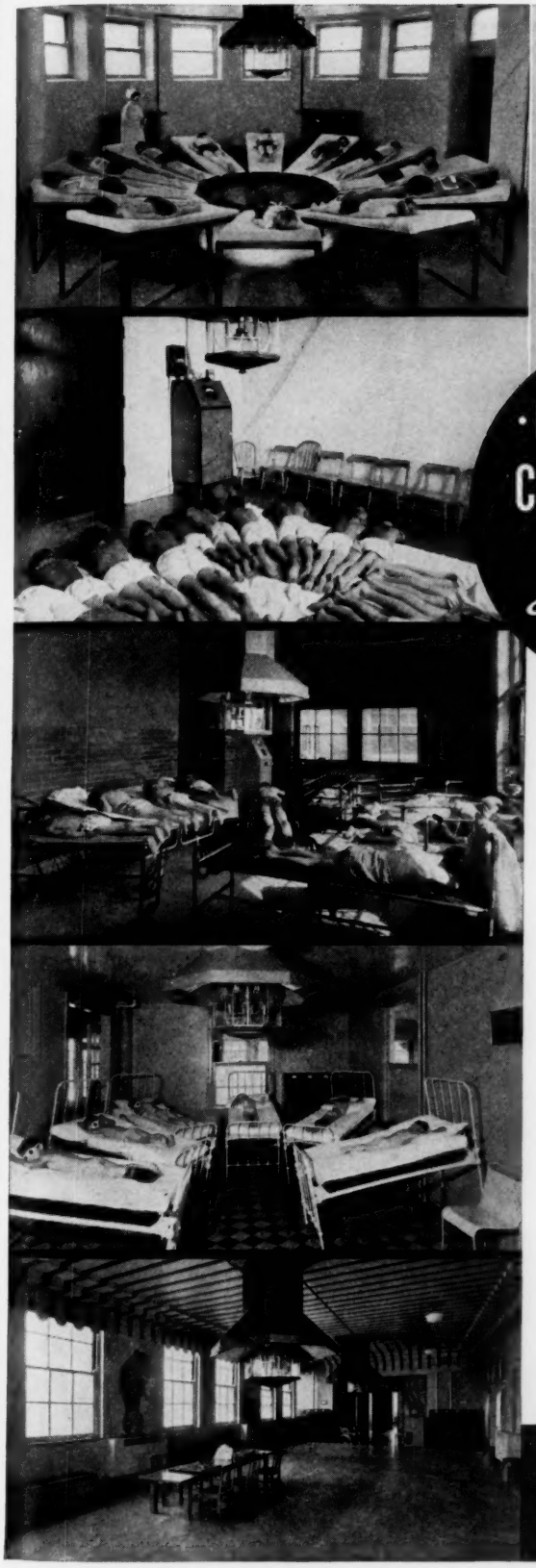
Squibb Vitavose—Malted wheat germ extract, 100 times richer in Vitamin B; 30 times richer in Vitamin G, than the best whole milk. Also rich in iron.

Squibb Dextro Vitavose (2 parts Dextrose, 1 part Vitavose)—Intended for modifying milk in infant feeding.

Squibb Chocolate Flavored Vitavose—Contains sucrose, Vitavose 30 per cent, cocoa, skim milk powder, lactose, vanilla. Makes a delicious milk drink, either hot or cold.

VITAVOSE

A SQUIBB VITAMIN B PRODUCT



HUNDREDS OF CHILDREN

get their daily sunshine under

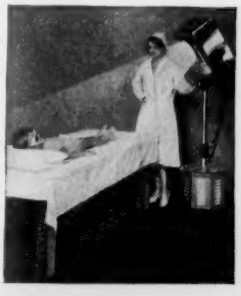
·EVEREADY· CARBON ARC *Solarium* UNITS

ONE-ARC, TWO-ARC and FOUR-ARC UNITS

THE Carbon Arc, as a source of artificial sunshine, available in all weather and all seasons, has been given nation-wide acceptance. Eveready Carbon Arc Solarium Units are used for group treatment in many children's hospitals, sanitariums and schools. Large groups of children are given daily irradiation, of natural sunlight intensity, under these highly efficient units. The character of the radiation can be adapted to the needs of the group by choice from five types of Eveready Carbons.

These carbon arcs provide radiation of uniform quality and intensity. No ultra-violet meter is needed. Motor driven, constant current arc control maintains uniform output. Full intensity is immediately available. Remote control and long burning period minimize attention.

The Eveready Professional Model Carbon Arc Lamp provides like advantages for individual treatment. Standard applicators can be attached to this lamp where the use of localized treatment is indicated.



Accepted by the Council on Physical Therapy of the American Medical Association

NATIONAL CARBON COMPANY, INC.
Carbon Sales Division, Cleveland, Ohio
Unit of Union Carbide UCC and Carbon Corporation
BRANCH SALES OFFICES
New York, Pittsburgh, Chicago, San Francisco

Golden Enamel Lined Cans
are just ONE reason why
STOKELY'S STRAINED FOODS
taste so much better

Golden enamel lined cans *do* make a difference. It's apparent the instant you open any one of Stokely's Strained Foods for Baby. They look, taste and even *smell* fresher, more naturally delicious, because—in these special cans—their finer quality is doubly protected against loss of color or flavor.

But there are other equally important reasons for the richer flavor, the absolute uniformity which make these foods so much more appealing to baby. Only choice, Stokely-grown vegetables and fruits are used. These are carefully prepared to retain flavor and food value in high degree—scientifically strained for smooth, even texture, then correctly seasoned with laboratory exactness. They go into the cans true, tempting, delicious, and the cans *keep* them that way.

That's why so many doctors are finding that Stokely's solve the problem of introducing strained foods into the infant's diet. They taste so good that baby takes them eagerly. Moreover, these better, protected foods are ready to heat and serve. That saves the mother time and trouble—assures more accurate following of your feeding instructions. Samples of these foods, including the new Strained Cereal, will gladly be sent to you upon request. Simply address Stokely Brothers & Co., 2241 South East St., Indianapolis, Ind.

Stokely's
Strained Foods *for* Baby
THE STRAINED FOODS BABY REALLY LIKES
Strained Green Beans, Tomatoes, Apricots, Carrots, Spinach, Prunes, Peas, Vegetable Soup, Cereal.
PROTECTED IN GOLDEN ENAMEL LINED CANS

Chemistry Challenges Custom!

INFANT FEEDING advanced with the advent of mixed sugars in artificial formulae. But, ounce for ounce, milk modifiers are more costly than milk. And many mothers believe the mixed sugars to be the more essential constituents of the formula. The cost of some milk modifiers is high—which over-emphasizes their value.

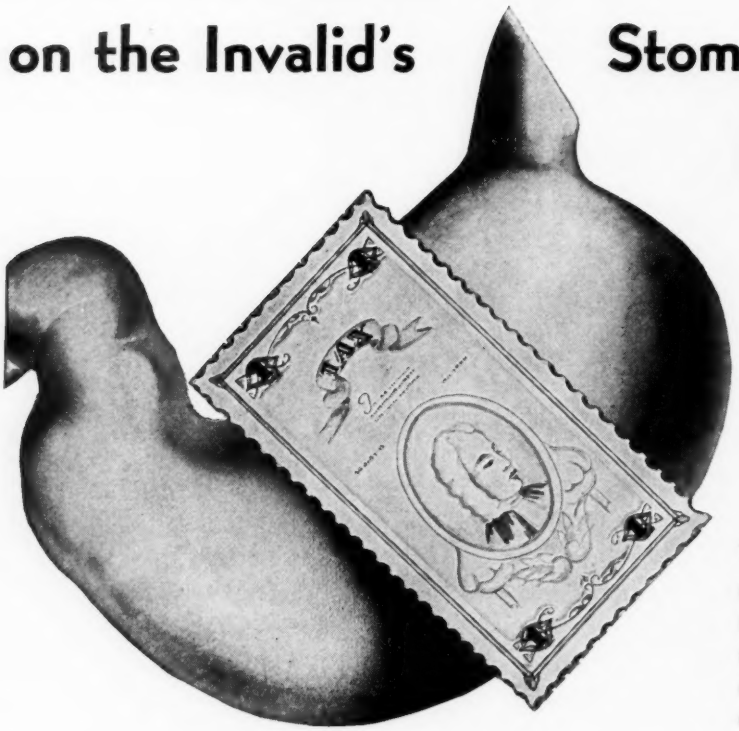
But modern Food Chemistry challenges this psychology. In Karo, maltose-dextrins are marketed as a food—and to-day mothers buy this milk modifier as a food, at food prices. The saving effected is up to 80%—when Karo is prescribed. The Corn Products Refining Co. charges for the constituents of Karo and nothing extra for the good name.

Prescribe Karo, the modern milk modifier. Karo Syrup is essentially Dextrins, Maltose and Dextrose, with a small percentage of Sucrose added for flavor. It is an ideal carbohydrate because it is well tolerated, readily digested, effectively utilized. Karo does not cloy the appetite, produce fermentation or disturb digestion.

Corn Products Consulting Service for Physicians is available for further clinical information regarding Karo. Please Address: Corn Products Sales Company, Dept. D-9, 17 Battery Place, New York City

NO ADDED TAX

on the Invalid's Stomach with KLIM



WHEN digestive tolerance is low, following illness or operation, here is a safe way to meet the increased food requirements of convalescence.

In everyday dishes, such as soups and cereals, simply include KLIM Powdered Whole Milk. Each tablespoonful of KLIM adds 42 extra calories with slight change in flavor, consistency or bulk.

KLIM is so digestible, so easily assimilable, that when used to fortify staple dishes it throws little extra burden on the weakened stomach. Most important, patients will welcome the wide variety of foods that can be made with KLIM. So different from the monotony of highly flavored, rapidly cloying "invalid drinks."

For your convenience in caring for convalescents, we have prepared a cookbook containing 70 recipes for dishes fortified with KLIM. Copies and a supply of KLIM will be gladly sent upon request.

ACCEPTED AMERICAN MEDICAL ASSN. Committee on Foods

KLIM

THE BORDEN COMPANY
Dept. 295, 350 Madison Ave., New York City

Please send me literature on the use of KLIM in convalescent feeding. Check here to receive sample. ☐

..... M.D.

Street .....

City ..... State .....

FOOD IN THE OPEN CAN

● One question commonly asked concerning canned foods is whether or not the contents of the can should be removed to another container immediately after opening. This question has its origin in the belief that if food is allowed to remain in the can after opening, it will absorb an injurious substance from the can and thus become hazardous to the health of the consumer.

For this belief there is not the slightest foundation of fact. Its origin probably lies in the old "ptomaine" concept of food poisoning. Why it should persist in the light of present day knowledge is a mystery. The belief that food must be emptied immediately from the can has been as thoroughly discredited as the "ptomaine" theory of food poisoning (1).

Food poisoning is usually caused by the ingestion of food containing certain bacteria or their metabolic products. It is, in most instances, the direct result of improper preparation, handling, or storage of food (2) (3).

We have previously described in these pages how all canned foods are subjected to thorough heat treatment which destroys not only pathogenic bacteria and their products, but also the most resistant organisms which may cause spoilage. Consequently, the freshly opened can is the cleanest container in the average kitchen.

There is, therefore, no reason from the standpoint of food poisoning why the food must be removed immediately after the can is opened. In addition, food will spoil no faster or no slower in the open can than in any other open container. The same precautions should be used in its preservation as are used for any other cooked food.

With certain foods, it is desirable from the standpoint of quality to remove the food from the can. Such foods, usually those of an acidic nature, may act slowly on the can after air is admitted and small amounts of tin and iron may be absorbed. The traces of these metals have been shown by a Government laboratory to be entirely innocuous (3), but iron in particular may impart a slight taste to the food.

Modern science has dispelled the old belief that, from the standpoint of health, food must be removed immediately from the can. The cooperation of the medical profession in dispelling this old and unfair prejudice against their products is earnestly solicited by the members of the American canning industry.

AMERICAN CAN COMPANY

230 Park Avenue, New York City

(1) Journal American Medical Association, 90, 459, 1573 (1928)

(2) Preventive Medicine and Hygiene, M. J. Rosenau, Appleton-Century Co., N. Y. 5th Edition

(3) Food-Borne Infections and Intoxications, F. W. Tanner, Twin City Printing Co., Champaign, Illinois

---

This is the fourth in a series of monthly articles, which will summarize, for your convenience, the conclusions about canned foods which authorities in nutritional research have reached. We want to make this series valuable to you, and so we ask your help. Will you tell us on a post card addressed to the American Can Company, New York, N. Y., what phases of canned foods knowledge are of greatest interest to you? Your suggestions will determine the subject matter of future articles.

The Seal of Acceptance denotes that the statements in this advertisement are acceptable to the Committee on Foods of the American Medical Association.

A LARGE FACTOR OF SAFETY

FOR every baby and child Irradiated Pet Milk provides a large factor of safety against a deficiency of vitamin D.

Every drop of Pet Milk is irradiated with ultra-violet rays, enriching it with vitamin D. A pint of Pet Milk, diluted with an equal part of water to make a full quart of extra-rich milk contains sufficient vitamin D to be the equivalent of 135 U.S.P. units of the vitamin D of cod-liver oil.

For a child past infancy this should be a sufficient supply of vitamin D when 1½ pints of whole milk is ingested daily.

PET MILK COMPANY *furnishes no formulae to the laity* • •

Irradiated Pet Milk is a most economical source, both of the milk ration and of vitamin D. It costs less generally than ordinary milk—is as safe as the best of certified milk—is more easily digested than any other form of milk.

Pet Milk is the original evaporated milk—a standard of highest quality for a full fifty years.

PET MILK COMPANY, 1441i Arcade Bldg., St. Louis, Mo.

Please send me, free of charge,

☐ **Samples of Irradiated Pet Milk** ☐ **Book prepared especially for physicians** ***"Irradiated Pet Milk—Its Character, Quality and Usefulness in Infant Feeding"*** **(includes formula)** ☐ **Pad of prescription blanks**

*Dr.*_____ *Address*_____

*City*_____ *State*_____

(Please attach your prescription form or letterhead to this coupon. Offer limited to physicians of Continental U.S.)

FOR EASY SHIFTING

Wise physicians keep infants on breast milk as long as possible and find it easy, when necessary, to shift them from breast milk to supplementary or to complete feedings of S. M. A.

Just as the skill of the modern motor car manufacturer produces an easy gear shift, so does the skill of the makers of S.M.A. produce a modern product so similar to breast milk that it is easy to shift from breast milk to S. M. A.

S.M.A. is thus used by many physicians as a supplementary feeding for infants who do not obtain enough breast milk. The composition is so similar that the daily shift is easy. S.M.A. is also used by many physicians after the child is taken from the breast. Again the shift is easy. Even when infants are deprived of breast milk shortly after birth, the transition to S.M.A. is usually very simple.

In the summer, when warm weather accentuates the problems of feeding, physicians readily and safely shift infants in their charge from breast milk to S. M. A.

BREAST MILK	COMPARATIVE ANALYSIS	S.M.A. (When diluted according to directions)
3.59%*	Fat	3.5% - 3.6%
1.23 - 1.5%*	Protein	1.3% - 1.4%
7.57%*	Carbohydrate	7.3 - 7.5%
0.215 - 0.226%*	Ash	0.25% - 0.30%
6.97†	pH	6.8 - 7.0
0.56‡	△	0.56 - 0.61
0.0023‡	Electrical Conductivity	0.0022 - 0.0024
1.032	Specific Gravity	1.032
68.0	Caloric Value per 100 cc.	68.0
20.0	Caloric Value per ounce	20.0

* Average per cent according to Holt, "American Journal Diseases of Children", Vol. 10, page 239, 1915.

‡ Friedenthal, H. -- Ueber die Eigenschaften kuenstlicher Milchsera und ueber die Herstellung eines kuenstlichen Menschenmilchersatzes. Zentralb. f. Physiol., Vol. 24, 1910, page 687.

† Davidsohn, H. -- Ueber die Reaktion, der Frauenmilch, Zeitsch. für Kinderh., Vol. 9, 1913, page 15.

S. M. A. is a food for infants—derived from tuberculin tested cows' milk, the fat of which is replaced by animal and vegetable fats including biologically tested cod liver oil; with the addition of milk sugar and potassium chloride; altogether forming an antirachitic food. When diluted according to directions, it is essentially similar to human milk in percentages of protein, fat, carbohydrates and ash, in chemical constants of the fat and in physical properties.

ACCEPTED AMERICAN MEDICAL ASSN

SAMPLES ON REQUEST

S. M. A. CORPORATION • CLEVELAND, OHIO

PARKE-DAVIS

HALIVER OIL

WITH VIOSTEROL

WAS THE SUMMER SUN ENOUGH?

Can vacation sunshine satisfy your patients' requirements for vitamin D for the entire year? Study of vitamin D storage in the human body indicates that the summer surplus is rapidly depleted.

Nor can we assume that the summer affords a reserve of vitamin A, the vitamin associated with maintenance of the integrity of mucous membranes. This factor should be supplied in abundance throughout the Fall and Winter seasons.

These two important vitamins, A and D, can be administered conveniently and palatably by means of Haliver Oil with Viosterol. This product is of particular advantage for use with infants and small children; the required dose can be dropped on the tongue or added to the food formula as desired.

Haliver Oil with Viosterol is supplied in 5-cc. and 50-cc. vials with dropper, and in 3-minim capsules, boxes of 25 and 100.

Twenty-five years' research experience in the development of vitamin preparations is reflected in the quality of Parke-Davis Haliver Oil preparations.

PARKE, DAVIS & COMPANY · Detroit

Preventing NUTRITIONAL ANEMIA *in Infants through a Normal* DIETARY REGIMEN

NUTRITIONAL anemia was present in 45% of the breast-fed and 51% of the bottle-fed in a group of more than 1,000 infants studied by Mackay.[1] Although this anemia was of mild degree, *it was sufficient approximately to double the morbidity among the artificially fed.*

Anemia Prevalent

Commenting on this work, the British Advisory Committee on Nutrition writes, "This form of anaemia is prevalent among infants, especially those living under conditions of city life, and is attributed to a deficiency of available iron and possibly also of copper. Its most important feature is susceptibility to infection, particularly a liability to colds, otorrhoea, bronchitis, and enteritis, and a tendency for infections to become chronic."[2]

	IRON	COPPER
Cow's Milk, 14 oz.	1.01 mg.	0.166 mg.
Dextri-Maltose With Vitamin B,* 1 oz.	2.40	0.570
	3.41	0.736
Daily Requirement**	3.11	"traces"

*Essentially maltose and dextrins with extracts of wheat embryo and yeast.

It is generally agreed that breast milk and particularly cow's milk are markedly deficient in iron and copper. But when 1 oz. of Dextri-Maltose With Vitamin B is added to 14 oz. cow's milk, properly diluted (as at 1 month), the above increase in iron and copper results.

Iron, incorporated in powdered milk, should be given as a routine to bottle-fed infants, according to the recommendations of this committee in a report to the Ministry of Health.

Milk Deficient in Iron

Stored in the liver of the full-term infant is a supply of iron and copper theoretically sufficient for the first six months of life. But actually the reserve is subject to wide variation,[1] probably because of variations in the iron content of the mother's diet during pregnancy. Hill, for example, says, "If the mother is anemic herself, or if she has eaten little iron-containing food during the last months of pregnancy, her offspring is born with an insufficient iron deposit. . . ."[3]

	IRON	COPPER
Cow's Milk, 20 oz.	1.44 mg.	0.24 mg.
Dextri-Maltose With Vitamin B, 1½ oz.	3.60	0.855
Pablum, ¼ oz.	2.10	0.09
	7.14	1.185
Daily Requirement**	4.18	"traces"

When ¼ oz. of Pablum is fed to the 3-months-old infant receiving 20 oz. cow's milk and 1½ oz. Dextri-Maltose With Vitamin B, a significant increase in iron and copper takes place.

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**The desirable iron intake for children, according to Rose *et al*, is 0.76 mg. per 100 calories. Infant of 1 month (8¼ lb.) and infant of 3 months (11¼ lb.), both require 50 calories per lb.[7]

[1-7] ***Bibliography on request.***

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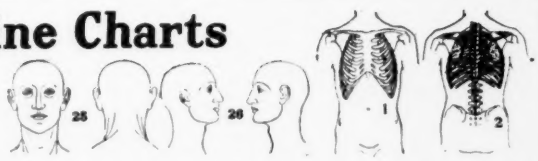

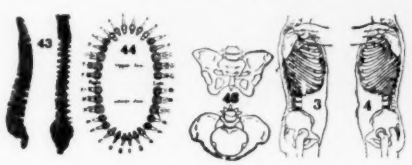

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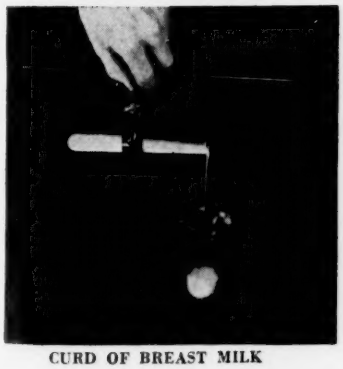

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*See Morse & Talbot: Diseases of Nutrition and Infant Feeding, pp. 48, 59, 61, 214, 215.

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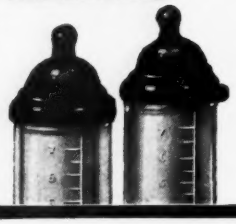

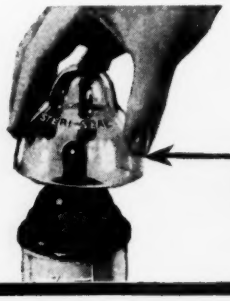

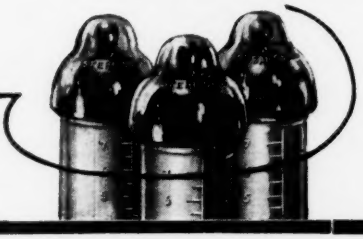

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"Grape sugar: In one-month baby, 8.6 grams per kilogram (Greenfield).

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"Levulose: (Lower for babies than adults.) One gram per kilogram (Keller).

"Maltose: Over 7.7 grams per kilogram (Reuss).

"Lactose: 3.1-3.6 grams per kilogram (Grosz).

"Cane sugar: Probably about the same as lactose (Reuss)."—*J. L. Morse, and F. B. Talbot: Physiology and pathology of the digestion of the carbohydrates in infancy, Boston M. & S. J., 164:852-855, June 15, 1911.*

1912

"Maltose has for many years been considered one of the most valuable of infant foods in modifying milk formulas but the German school in the last few years has called special attention to the value of this sugar as a substitute for milk and cane sugars in conditions of intestinal fermentation. It is more easily assimilated and more rapidly absorbed than lactose or saccharose and it may be taken therefore by the infant in larger quantities without producing sugar fermentation."

"Maltose is especially indicated in the feeding of very young and delicate infants, and in all cases where either milk or cane sugar has produced intestinal fermentation and sugar intoxication. In the feeding of maltose it has been found advisable to combine it with about equal parts of dextrin. In Germany, and later in this country, 'Soxhlet's Nahrzucker' (which contains maltose 52.44 per cent., dextrin 41.26 per cent., and sodium chlorid 2 per cent.) has been largely used. Mead's Dextri-Maltose (malt sugar), which contains about equal parts of dextrin and maltose, is a similar preparation which may be used instead of milk sugar or cane sugar for modifying milk mixtures."—*B. K. Rachford: Diseases of Children, D. Appleton & Co., New York, 1912, p. 125.*

1913

"It is well to start with one ounce (albumin milk, or albumin-buttermilk) to every pound of body-weight in the twenty-four hours, increasing gradually until two or three ounces to the pound of body-weight are being given. Then add sugar, preferably a malt sugar, about one-fourth of an ounce at a time to the twenty-four-hour quantity, until an ounce or an ounce and a half is being given."—*J. Foote: Principles of treatment in malnutrition and atrophy of infants, Interstate M. J., 20:1918, No. 6.*

1914

"Milk sugar and cane sugar may be used in infant feeding, but my preference is for malt sugar. Mead and Johnson put up a convenient preparation which they call Dextri-Maltose and which consists of maltose 51 per cent., dextrin 47 per cent., sodium chloride 2 per cent., and which has a food value of about 110 calories per ounce."—*J. A. Gannon: Whole milk dilutions in feeding normal infants, Washington Med. Annals, 13:38-43, Jan., 1914.*

1914

"Dextrin-maltose causes the greatest gain in weight, cane sugar less, and lactose produces the least gain."—*M. S. Reuben: Observations on milk station infants, Arch. Pediat., 31:176-196, March, 1914.*

1914

"A composite opinion of the sugars is in favor of dextri-maltose, milk sugar and cane sugar in the order named."—*R. A. Strong, Essentials of modern artificial feeding of infants, Lancet-Clinic, March 14, 1914.*

1914

"Experiments show that sugars vary in their rate of absorption, some being assimilated rapidly, while others distribute their nutriment over a longer period. For example, maltose is most promptly assimilated, cane sugar next and milk sugar slowest."

"The condition in which dextri-maltose is particularly indicated is in acute attacks of vomiting, diarrhea and fever. It seems that recovery is more rapid and recurrence less likely to take place if dextri-maltose is substituted for milk sugar or cane sugar when these have been used, and the subsequent gain in weight is more rapid.

"In brief, I think it safe to say that pediatricians are relying less implicitly on milk sugar, but are inclined to split the sugar element, giving cane sugar a place of value, and dextri-maltose a decidedly prominent place, particularly in acute and difficult cases."—*W. D. Hoskins: Present tendencies in infant feeding, Indianapolis M. J., July, 1914.*

1915

"In the severe cases (of diarrhea) he (Benson) uses Finkelstein's casein milk with malt sugar. He also believes that dextri-maltose is to be preferred to milk sugar or any other sugar, as the infants gain more rapidly and digest more easily this form of sugar."—*R. A. Benson: Observations on 1,500 artificially-fed infants, Med. Century, Feb., 1915, p. 33; abst. Arch. Pediat., 32:556-557, July, 1915.*

1915

"Until very recently we have taken it for granted that milk sugar was the best, but now many consider that malt sugar is even better. However, the malt sugar is not used in its pure state, but in the form of extracts, as dextri-maltose."—*E. B. Lowry: Your Baby, Forbes & Co., Chicago, 1915, p. 162.*

1915

"Cane-sugar (saccharose), like most of the other disaccharids, is not absorbed as such, but must first be split by the invertase of the intestinal secretion into the two glucoses, dextrose and levulose, which are readily absorbable. Maltose (malt-sugar) occupies an exceptional position among the disaccharids, in being partly absorbable as such. This is probably due to the fact that it can be split not only by the maltase of the digestive juices, but also by the same ferment being present and active in the circulating blood (Chittenden and Mendel)."

"Anticipating a little, we may mention that all cases, in which lactose may advantageously be replaced by other carbohydrates, are pathological, and without exception the result of unsuccessful attempts at artificial feeding; they will therefore be discussed under that head.

"Dextrin, intermediate between sugar and starch, is physiologically nearer to the former; we shall have occasion to see that, under certain conditions, it may supplement sugar very advantageously. Given together with maltose, it materially delays the fermentation of the latter; Stolte observes that the more complex the carbohydrate the longer fermentation is postponed."

"All malted foods contain dextrin, and there is reason to believe that their value largely depends on their being somewhat complicated; such, at least, is the opinion of Usuki and Stolte, who believe that a mixture of carbohydrates is more slowly absorbed than a pure sugar, and therefore tends to check fermentation in the intestine. Southworth explains the matter more definitely, by attributing the antifermentative action entirely to the dextrin, which is not fermentable as such, but only after it has been split into maltose, a process that takes place only gradually, and in the later stages of digestion."

"I make it a rule to give the ordinary formula with dextrin-maltose whenever the usual milk or cane-sugar mixtures seem to cause excessive fermentation and colic, or are attended with the evacuation of soap stools. I decidedly prefer this, as a preliminary measure, to going over at once to some very low fat combination, which can only be a temporary makeshift at best. I also find dextrin-maltose an excellent addition to albumin-milk when the first object of that food has been achieved and a gain in weight is desired; in this way I have succeeded in feeding albumin-milk far beyond the period usually advised, with highly gratifying results."—*F. L. Wachenheim: Infant-Feeding; Its Principles and Practice, Lea & Febiger, Phila., 1915, pp. 31, 33, 146, 158.*

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